

THE MEDICAL JOURNAL OF AUSTRALIA

VOL. I.—48TH YEAR

SYDNEY, SATURDAY, APRIL 29, 1961

No. 17

Table of Contents

[The Whole of the Literary Matter in THE MEDICAL JOURNAL OF AUSTRALIA is Copyright.]

ORIGINAL ARTICLES—	Page	BRITISH MEDICAL ASSOCIATION—	Page
The Acute Cholestatic Syndrome, by R. A. Joske, L. R. Finlay-Jones and E. G. Saint .. .	609	Victorian Branch: Section of Preventive Medicine .. .	634
The Management of Tetanus, by B. S. Clifton .. .	618	OUT OF THE PAST .. .	634
A Miniature Pace-Maker for Direct Stimulation of the Myocardium, by Douglas Cohen, Victor Hercus, A. C. Bowring and E. C. Hulme .. .	624	SPECIAL CORRESPONDENCE—	
REPORTS OF CASES—		London Letter .. .	634
Chlorpromazine Given Orally in the Treatment of Severe Tetanus: A Case Report, by I. Maddocks and J. K. Dawborn .. .	625	CORRESPONDENCE—	
REVIEWS—		Erythroblastosis Fœtalis—Random Thoughts .. .	636
Gynecological Therapy .. .	626	Frequency of Compulsory Medical Examinations under N.S.W. Workers' Compensation Rules .. .	636
General Anaesthesia .. .	626	Furaltadone—A Clinical Trial .. .	636
Disc Lesions and Other Intervertebral Derangements .. .	627	Storage and Supply of Immunizing Material .. .	637
Fluid Balance in Obstetrics .. .	627	Hypertension and Life Assurance .. .	637
Queensland Year Book, 1959 .. .	627	POST-GRADUATE WORK—	
Addendum 1960 to the British Pharmacopœia, 1958 .. .	627	The Post-Graduate Committee in Medicine in the University of Sydney .. .	638
The Development of the Infant and Young Child .. .	628	The Melbourne Medical Post-Graduate Committee .. .	639
Atlas and Manual of Dermatology and Venereology .. .	628	Cardiac Society of Australia and New Zealand .. .	639
BOOKS RECEIVED .. .	628	DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA .. .	639
LEADING ARTICLES—		NOTES AND NEWS .. .	639
The Plunket Society .. .	629	THE COLLEGE OF RADIOLOGISTS OF AUSTRALASIA—	
CURRENT COMMENT—		Examinations for Diploma .. .	640
The Treatment of Severe Tetanus .. .	630	NOTICE—	
Spent Radon Seeds .. .	631	Third John Irvine Hunter Memorial Oration .. .	640
Increasing Interest in Child Development .. .	631	NOMINATIONS AND ELECTIONS .. .	640
ABSTRACTS FROM MEDICAL LITERATURE—		DEATHS .. .	640
Surgery .. .	632	DIARY FOR THE MONTH .. .	640
BRUSH UP YOUR MEDICINE—		MEDICAL APPOINTMENTS: IMPORTANT NOTICE .. .	640
The Early Management of Severe Tetanus .. .	634	EDITORIAL NOTICES .. .	640

THE ACUTE CHOLESTATIC SYNDROME.

By R. A. JOSKE, M.D., M.R.A.C.P.,¹
L. R. FINLAY-JONES, M.B., D.C.P., M.C.P.A.,

AND

E. G. SAINT, M.D., F.R.A.C.P.,

From the Department of Medicine, University of Western Australia, and the Department of Pathology, Royal Perth Hospital, Perth, Western Australia.

THE occasional presentation of patients with the clinical and biochemical features usually associated with biliary obstruction, but in whom no mechanical biliary obstruction can be demonstrated at operative or autopsy examination, has been recognized for many years. With increased understanding of the clinical syndromes of hepato-biliary disease, it has been realized that many of these patients fall into well-defined disease entities such as primary (xanthomatous) biliary cirrhosis, Gilbert's disease or the Dubin-Johnson syndrome (Ahrens *et alii*, 1950; Dubin and Johnson, 1954; Sprinz and Nelson, 1954; Cameron, 1958; Foulk *et alii*, 1959). In other instances the jaundice follows, and is clearly related to, the administration of drugs, and a large number of substances in common therapeutic use has been incriminated in this respect (Klatskin, 1956).

¹Adolph Basser Research Fellow in Medicine, Royal Australasian College of Physicians.

However, there remain further patients in whom "pseudo-obstructive" jaundice arises without any such recognized cause. These have been described under various names, including cholangiolitic hepatitis, intra-hepatic obstructive jaundice, cholestatic hepatitis, primary pericholangitis and hepatitis with pseudo-obstruction or manifestations simulating obstruction. None of these terms is entirely satisfactory. The term "cholangiole" has been used in different senses by different authors. Considerable doubt exists as to whether the primary lesion affects the parenchymal cells or the smaller bile passages, and whether it is in fact inflammatory in the sense implied by "hepatitis". It is also probable that these terms have been used to describe different diseases by different authors. We have therefore preferred in this paper the non-specific term "cholestatic syndrome".

Recent study of the cholestatic syndromes dates largely from the classical paper of Watson and Hoffbauer (1946) who fully reviewed the earlier literature and reported eight further cases of "cholangiolitic hepatitis". Their patients included five males and three females, whose ages ranged from nine to 69 years. They noted the clinical resemblance of the onset of this disease to that of viral hepatitis, and considered, on epidemiological and clinical grounds, that it might in some instances be a variant of viral hepatitis, a suggestion first made by Eppinger in 1937. They considered the outstanding feature of the disease to be jaundice lasting for months or even years, and thought it to carry a poor prognosis. One of their eight patients died.

Review of this paper in the light of later experience suggests that Watson and Hoffbauer grouped together

two slightly different syndromes: (i) prolonged hepatitis with evidence of hepato-cellular damage, and "obstructive" manifestations shown by a high serum alkaline phosphatase level and a high cholesterol level (for example, Cases II and III); and (ii) a type of prolonged jaundice with no evidence of hepato-cellular damage, but also with obstructive manifestations in the absence of external biliary obstruction (for example, Cases I and VI).

Several other authors have since described patients of the first type, including Eliakim and Rachmilewitz (1956), Popper and Szanto (1956), Goldgraber and Kiraner (1959) and Overholt and Hardin (1959). This disease is now termed cholangiolitic hepatitis, and is recognized as a distinctive pattern of liver disease usually evoked by viral hepatitis. Steigmann and Popper (1943) had previously found complete biliary obstruction occurring in 10% of patients with acute hepatitis. It is characterized by chronic jaundice without external biliary obstruction, but with biochemical features of mild parenchymal cell damage and of biliary "pseudo-obstruction", shown by hypercholesterolemia and an increased serum alkaline phosphatase level. The prognosis is uncertain, for in a proportion of cases cholangiolitic hepatitis may progress to cirrhosis, although most patients recover after weeks or months of jaundice (Watson and Hoffbauer, 1946).

Less attention has been paid to the smaller group of patients with pseudo-obstruction and no detectable evidence of parenchymal cell damage. Dible, McMichael and Sherlock (1947) reported two such cases in elderly females, as well as three other patients in whom "obstructive" jaundice persisted, despite adequate surgical relief of an extrahepatic biliary obstruction. They noted low alkaline phosphatase values (below 30 King-Armstrong units) and the absence of hyperglobulinemia. Three of the five patients died, all with evidence of nitrogen retention. Histologically there was evidence of bile retention without inflammation within the liver. Four somewhat similar cases in younger patients in their fourth decade were described by Björneboe, Iversen and Trautner (1952). They included two males and two females, all exhibiting negative results of flocculation tests and normal serum alkaline phosphatase levels. All improved after operation. Liver biopsies showed extensive bile plugging but minimal inflammatory change. Shaldon and Sherlock (1957) reported a further 12 such cases, seven males and five females, with prolonged benign jaundice, and in the majority, negative flocculation test results and only slight increases in serum alkaline phosphatase levels. Liver biopsies from 10 patients showed hepatitis with an unusual degree of bile retention. They considered the disease to be a variant of viral hepatitis. Similar cases have been recorded by Lipschutz and Capson (1955), Johnson and Doenges (1956) and Overholt and Hardin (1959).

The two patients, one male and one female, reported by Summerskill and Walshe (1959) exhibited a somewhat different type of pseudo-obstructive jaundice. The serum bilirubin level reached 40 mg. per 100 ml., and jaundice recurred without apparent cause for periods of weeks or months. Both patients showed raised serum alkaline phosphatase levels and negative flocculation test results. Liver biopsies showed an "obstructive" picture.

Scandinavian workers have described a similar type of jaundice associated with pregnancy (Svanbourg, 1954; Thorling, 1955; Svanbourg and Ohlsson, 1959), which they have named "recurrent jaundice of pregnancy". They observed patients who developed progressive jaundice associated with itching of the skin, dark urine and pale feces during the last four months of pregnancy. Investigations showed moderate increases in serum bilirubin levels (to 6 mg. per 100 ml.) and alkaline phosphatase levels (up to 40 Buch units); serum protein levels were normal and flocculation tests gave negative results. Liver biopsies showed multiple bile thrombi, but minimal other changes. There was no evidence of external biliary obstruction. Delivery was followed by

complete clinical and biochemical recovery, although the jaundice recurred with subsequent pregnancies.

It should be noted that jaundice arising from methyl testosterone, norethandrolone, chlorpromazine and related drugs also presents this clinical and laboratory picture (Werner, Hanger and Gritzler, 1950; Zatuchni and Miller, 1954; Azima and Ogle, 1954 and later papers). Post-arphenamine jaundice varies somewhat, and it appears that flocculation tests are very variable in this entity (Hanger and Gutman, 1940). It merits further experimental study by modern methods.

A detailed study of the pathology of liver biopsy specimens in typical viral hepatitis, cholangiolitic hepatitis and obstructive jaundice was presented by Gall and Braunstein (1955). They held strongly that the hepatic lesions of cholangiolitic hepatitis are "not clearly distinguishable" from those of viral hepatitis, and that the occasional features of intrahepatic obstruction merely represented "a circumstance of coincidence". However, this paper is open to criticism. Of the 14 cases presented, 10 gave strongly positive results to flocculation tests, while the serum alkaline phosphatase level was elevated in only five of the 11 cases in which it was measured. It would appear that most of these patients had not "cholangiolitic hepatitis", but viral hepatitis with unusually prolonged jaundice and consequent malnutrition and lipid changes. The average age of the group with cholangiolitic hepatitis was 50 years: it has been shown that the course of infectious hepatitis in the elderly patient is frequently atypical, with prolonged jaundice and considerable debility (Saint, 1952), and that the alkaline phosphatase level is higher than in younger patients (Eliakim and Rachmilewitz, 1956). A more recent review of the pathology of "cholestatic hepatitis" by Dubin (1956) suggested that, although it may well be a form of viral hepatitis, the histological appearances closely resemble those of obstructive jaundice, and a differential histological diagnosis of biopsy material would be possible to "a pathologist with considerable experience" in only about 70% of cases. Similar views have been expressed by Popper and Schaffner (1959).

The role of steroids in the diagnosis and treatment of liver disease has been studied extensively in the past few years. Solem and Olsen (1955) found that corticotrophin (ACTH) caused a rapid fall in serum bilirubin levels in acute hepatitis, but not in jaundice resulting from external biliary obstruction. They thought this might be used as a test in the differential diagnosis of jaundice. Their findings have been questioned by some (Chalmers *et alii*, 1956; Katz, Ducci and Alessandri, 1957), but recently have been confirmed by Summerskill and Jones (1958).

The use of steroids in the treatment of cholangiolitic hepatitis was suggested by Lipschutz and Capson (1955), although they did not use them. However, Sborov *et alii* (1954), in six cases, and Johnson and Doenges (1956) in two cases, reported an immediate response to ACTH in young men with cholangiolitic hepatitis which was probably the result of viral hepatitis. Similar findings have been recorded by Overholt and Hardin (1959). On the other hand, Shaldon and Sherlock (1957) and Goldgraber and Kiraner (1959) considered that in subacute and chronic cholangiolitic hepatitis steroids have little, if any, effect upon the progression of the basic hepatic pathology, although they may produce temporary symptomatic and biochemical improvement. This had also been observed by Last (1957) in active chronic hepatitis. This controversy springs largely from use of the term "cholangiolitic hepatitis" to cover different clinical entities. It would appear that in the acute cholestatic syndrome without active parenchymal cell damage, steroids may hasten the disappearance of jaundice, but that when the progressive changes leading to cirrhosis have begun, the response to steroids is as poor in "cholangiolitic hepatitis" as Last (1957) found in chronic progressive viral hepatitis.

It is apparent from this review of the literature that there exist serious gaps in knowledge of the acute cholestatic syndrome, partly factual and partly due to the imprecise use of names such as cholangiolitic hepatitis. It is well recognized as being of diverse aetiology, but of the various agents discussed, only chemicals, pregnancy and viral infection are well substantiated. There is some doubt as to the pathology and the use of liver biopsy in diagnosis, and, more generally, of the pathogenesis of the disease. The prognosis is considered to be poor, although the great majority of reported cases has recovered uneventfully. Nor is there much information concerning the value of serum glutamic-oxaloacetic transaminase (SGOT) estimations in the acute cholestatic syndrome. For these reasons the present paper reports 15 further patients with the acute cholestatic syndrome who have been examined by us, and discusses the diagnosis and natural history of this disease. Patients with acute cholestasis following treatment with the various drugs known to cause jaundice have not been included in this report, nor have patients with subacute or chronic hepatitis associated with unusually high alkaline phosphatase levels. These have been adequately described elsewhere.

The clinical and laboratory methods used have been discussed in a previous paper, which also made brief mention of two of the present cases (Saint *et alii*, 1953). Since the various flocculation tests were highly similar in any particular patient, these have been considered together for convenience. Those used were the cephalin-cholesterol and thymol flocculation tests, the thymol turbidity test and the zinc sulphate test. Serum glutamic-oxaloacetic transaminase estimations were performed by the method of Cabaud, Leeper and Wroblewski (1956).

Clinical Observations.

The diagnosis of acute cholestasis was made in 15 cases which satisfied the following criteria: the presence of jaundice with negative flocculation test results and the absence of mechanical obstruction of the biliary tract (shown at operation or by direct cholangiography, and by the subsequent course of the disease and investigations after the subsidence of the jaundice). Cases have not been included in which later evidence of biliary or pancreatic disease was obtained, or where there was any history suggesting the administration of hepatotoxic drugs before the onset of jaundice. The 15 patients studied were examined by us during the period from 1949 to 1960 inclusive, but our clinical material is too selective to allow any useful estimate of the frequency of the acute cholestatic syndrome.

The salient clinical and laboratory findings are listed in Table I.

The outstanding clinical observation was the difference between the behaviour of the disease in the two sexes. The males were in general older, their ages ranging from 37 to 64 years (average 50 years), compared with a range of 23 to 39 years (average 31 years) in the females. This difference was emphasized by other features; itching and weight loss were relatively more frequent in males, in whom the degree of jaundice was greater and its duration correspondingly longer, the average figures being approximately 11 and 6 weeks respectively. It may be relevant that five of six females showed significant hyperglobulinemia, but only two of nine males did so, and that the only acute fatality occurred in a male patient. In the females, too, there was a striking relation to pregnancy in four. Two (Cases XI and XII) were in the second trimester of pregnancy at the time of onset of the jaundice, and their illness corresponds in many respects with that described by Svanborg (1954). Two others (Cases X and XIII) had received blood transfusions for obstetrical mishaps four months before the jaundice appeared. The fifth female patient (Case IX) had one child, aged six years, but had not conceived after this, although she had normal menses, while the final female patient had not been pregnant for two years prior to the onset of jaundice. She had had nine pregnancies, none of them accompanied by jaundice.

The onset of the disease closely resembled that of viral hepatitis. Three patients had unequivocal contact with viral hepatitis a few weeks before the onset of jaundice, and three others had received recent blood transfusions. The development of symptoms was gradual. An initial period of vague ill health with undue fatigability, minor digestive disturbances and weight loss was followed after a few days or weeks by the development of anorexia, nausea, vomiting and jaundice. Severe constitutional symptoms preceded the onset of jaundice in nine patients, and in the remainder both occurred at the same time. These constitutional symptoms varied—malaise, anorexia, nausea and vomiting were considerable in all except one patient. Two also had diarrhoea. Pain was a frequent complaint, usually being felt in the epigastrium or right hypochondrium and being described as "sore" or "burning" in character. Muscle and back pain were occasionally present. No patient had biliary colic.

However, jaundice was the outstanding symptom and the one leading to hospital admission in all cases. It was clinically obstructive in type, with itching of the skin. In four cases there were definite spontaneous fluctuations in the depth of the jaundice with corresponding changes in the colour of the stools, which led to considerable diagnostic difficulty.

The duration of the disease before admission to hospital varied from a few days to three months, but was usually about five weeks. The referral or admission diagnoses varied. In seven cases an initial diagnosis of viral hepatitis was based on epidemiological and clinical evidence; pronounced upper abdominal discomfort led to a diagnosis of cholelithiasis in three, and considerable weight loss in three males, aged 54, 60 and 64 years respectively, to one of carcinoma of the pancreas, while another was thought to have portal cirrhosis. The final patient was referred with the non-committal diagnosis of "jaundice for investigation".

The initial clinical examination revealed jaundice and evidence of weight loss. Fever was unusual, although five patients had slight pyrexia; three had bradycardia. Enlargement of the liver was detected in 13 and splenomegaly in four cases. The liver was firm, smooth and usually slightly tender to palpation. Ascites was present in one patient (Case V). In all cases the faeces were pale and choluria was present. None of the patients showed the stigmata of chronic liver disease, nor was the gall-bladder palpable in any instance.

Initial Laboratory Investigations.

The initial biochemical results are shown in Table I. In all cases the serum bilirubin level was increased and the flocculation tests gave negative results. Elevation of the serum alkaline phosphatase level occurred in 12 of the 15 cases, but in five only did it exceed the level of 30 King-Armstrong units used arbitrarily to distinguish parenchymal from obstructive jaundice, and in one only was the elevation gross (Case V). As would be expected from the negative flocculation test results, changes in serum protein levels were slight, although minor depression of the serum albumin level and elevation of the serum globulin level were occasionally present. The results of protein electrophoretic studies were unremarkable.

Other initial investigations were not of value in the differential diagnosis. Only one patient had significant anaemia, and none had a peripheral leucocytosis. Radiological examinations revealed no diagnostic features, although enlargement of the liver or the spleen was occasionally noted.

Estimations of the SGOT level were obtained in the case of six patients examined in the last two years, and in five the values were grossly elevated (Table I) and led to a correct diagnosis of hepato-cellular jaundice despite the other features suggesting biliary obstruction. This is even more apparent if the SGOT: alkaline-phosphatase ratio is calculated as suggested by Latner and Smith (1958), the values of 12.4 (Case VIII), 10.0 (Case IX), 21.7 (Case XI), 8.3 (Case XIII) and 10.8 (Case XIV) lying well beyond the range indicative of obstructive

TABLE I.
Clinical and Initial Biochemical Findings in Fifteen Patients with the Acute Cholestatic Syndrome.¹

Case Number.	Sex.	Age. (Years).	Contact with Hepatitis.	Itching of Skin.	Weight.	Diet.	Enlargement of Liver (cm.).	Enlargement of Spleen.	Admission Diagnosis.	Initial Biochemical Results.					Liver Biopsy.	Operation.	Duration of Icterus (Weeks).	Complications, Treatment and Result.
										S.B.	A.P.	F.	A.	G.				
I	M.	42	Yes.	Yes.	Loss 28 lb.	Good.	0	0	Viral hepatitis.	17.5	26	Neg.	4.1	2.3	—	Yes.	17	Full recovery.
II	M.	44	No.	Yes.	Loss 20 lb.	Good.	3	0	Viral hepatitis.	25	12	Neg.	5.2	2.9	—	Yes.	13	Full recovery.
III	M.	37	Yes.	Yes.	Little change.	Good.	5	+	Viral hepatitis.	10	23	Neg.	4.3	2.6	—	Yes.	17	Full recovery.
IV	M.	61	No.	No.	Loss 5 lb.	Chronic alcoholic.	3	0	Stone in common bile duct.	18	46	Neg.	3.1	2.0	—	Yes.	11	Associated acquired hemolytic anemia (see text).
V	M.	46	No.	No.	Loss, ? amount.	Good.	3	0	Cirrhosis of liver.	25	70	Neg.	3.5	2.4	—	Yes.	8	Death after laparotomy with hepato-renal failure (see text).
VI	M.	60	No.	Yes.	Loss 20 lb.	Good.	2	0	Carcinoma of pancreas.	10.1	40	Neg.	4.1	3.3	—	Yes.	4	Full recovery.
VII	M.	52	Yes.	Yes.	Little change.	Good.	2	0	"For investigation."	20.3	23	Neg.	3.4	3.6	—	No.	9	Full recovery.
VIII	M.	54	No.	Yes.	Loss 14 lb.	Good.	5	+	Carcinoma of pancreas.	10.3	16.5	Neg.	3.2	2.9	205	Yes.	10	Full recovery after perforated duodenal ulcer.
IX	M.	64	Transfusion 3 months before.	Yes.	Loss, ? amount.	Good.	4	0	Carcinoma of pancreas.	18.2	19.8	Neg.	2.3	3.6	197	Yes.	10	Full recovery.
X	F.	27	No.	?	Gaining.	Good.	1	0	Viral hepatitis.	6.3	20	Neg.	3.3	3.6	—	Yes.	8	Full recovery.
XI	F.	39	Transfusion 4 months before.	No.	Loss 14 lb.	Good.	3	0	Viral hepatitis.	4.9	9.4	Neg.	4.0	3.8	204	Yes.	9	Full recovery.
XII	F.	20	No.	Yes.	Little change.	Good.	0	0	Cholelithiasis.	5.8	33	Neg.	3.8	2.2	—	Yes.	5	Normal labour and baby. Recovery.
XIII	F.	23	No.	Yes.	Gaining (pregnant).	Hypertension gravidarum.	2	0	Viral hepatitis.	6.0	26	Neg.	3.1	3.7	215	No.	16+	Normal labour and baby. Lost to follow-up while still icteric.
XIV	F.	33	Transfusion 4 months before.	No.	Little change.	Good.	3	+	Viral hepatitis.	11.0	34	Neg.	4.0	4.0	368	Yes.	4	Full recovery (see text).
XV	F.	36	No.	Yes.	Little change.	Good.	2	+	Cholelithiasis.	12.8	6.6	Neg.	2.9	5.3	21	Yes.	6	Full recovery.

¹ S.B. = serum bilirubin level in milligrammes per 100 ml.

A.P. = serum alkaline phosphatase level in King-Armstrong units.

F. = results of flocculation tests.

A. = serum albumin level in grammes per 100 ml.

G. = serum globulin level in grammes per 100 ml.

SGOT. = serum glutamic-oxaloacetic transaminase levels in units.

jaundice. On none of these five patients was diagnostic laparotomy performed, although in Case VIII operative intervention was necessitated by the perforation of a duodenal ulcer during convalescence, and the patient of Case IX was first examined by us after operation. In the sixth patient (Case XV) both alkaline-phosphatase and SGOT levels were normal, and laparotomy was undertaken. However, in general, these findings add further support to the value of SGOT estimations in the differential diagnosis of acute jaundice. Their pathogenetic significance is discussed below.

Liver Biopsy.

Diagnostic aspiration biopsy of the liver was performed in eight cases, in three (Cases I, II and IX) upon two occasions. Operative biopsies were obtained from eight patients, but in Case III this specimen was unavailable for review. Eighteen specimens were thus available for examination, and the histological appearances are summarized in Table II.

In no instance was there any significant derangement of liver architecture in the biopsy material. However, post-mortem examination in Case IV showed the changes of post-necrotic scarring four years after the initial episode of cholestasis.

The portal tracts showed as a constant feature an increase in fibroblasts (Figure 1).¹ This occurred in cases

in which the biopsy was obtained within two or three weeks of the onset of jaundice, as well as in those in which it had been present for much longer. At the periphery of the lobules there was often fibroblastic proliferation and leucocytic infiltration amongst the parenchymal cells (Figure II). Leucocytes were conspicuous in the portal tracts, and were predominantly polymorphonuclear leucocytes or lymphocytes—often a mixture of both—and were occasionally accompanied by eosinophils (Figure II). Bile ductule proliferation was inconstant and never excessive; dilatation and biliary stasis were not observed in these channels.

The parenchymal cells showed striking evidence of bile retention in most cases. Bile thrombi in the biliary canaliculi were often as abundant as those seen in jaundice from extrahepatic biliary obstruction (Figure III). They were most numerous in the centrilobular zone, as were swollen parenchymal cells, and also Kupffer cells containing intracytoplasmic bile granules (Figure IV). Bile lakes were not seen. Distributed haphazardly in the lobules were parenchymal cells, either singly or in small groups, showing ballooning or eosinophilic degeneration, so that in a low-power view these respective large and small cells made the liver columns appear disorderly (Figure V). There were occasional areas where a collapsed reticulin framework and engorged sinusoids indicated the disappearance of parenchymal cells (Figure VI). Polymorphonuclear leucocytes were present in

TABLE II.
Summary of Histological Appearances in Seven Operative and Eleven Aspiration Liver Biopsies from Thirteen Patients with the Acute Cholestatic Syndrome.¹

Case Number.	Duration of Jaundice. (Weeks.)	Portal Tracts.			Parenchymal Cells.						
		Leucocytes.	Bile Ductule Proliferation.	Fibroblasts.	Bile Thrombi.	Bile Granules.	"Ballooned" Cells.	Multi-nucleated Cells.	Eosinophilic Necrosis.	Mitotic Activity.	Fat.
I (a)	5	—	—	+	—	+	+	+	—	—	—
(b)	10	—	—	+	+	++	++	++	—	—	—
(c)	11.5	+ Lymphocytes + Polymorpho- nuclear leuco- cytes	+	+	+	+	+	+	—	—	—
II (a)	5	—	—	+	+	+	+	++	—	—	—
(b)	6.5	+ Polymorpho- nuclear leuco- cytes	—	+	++	—	+++	+++	++	—	—
(c)	11	—	—	+	—	+	—	+	—	—	—
III	8	+ Lymphocytes	—	+	+	++	++	+++	—	—	—
IV (Operative)	3	+ Lymphocytes + Polymorphs	+	++	++	+	+++	++	—	—	+++
V (Operative)	5	—	—	—	++	+	+	++	—	—	+
VI (Operative)	2	+ Lymphocytes + Eosinophils	+	+	+++	—	—	—	+	—	—
VIII	5	++ Lymphocytes +++ Polymorphs	+	+	—	++	++	++	+	++	—
IX (Operative)	5	+++ Polymorphs + Eosinophils + Lymphocytes	+	++	++	+	++	+	++	+	—
X (a)	6	++ Polymorphs + Eosinophils	+	+	++	++	+	—	++	+	—
(b)	10	+ Polymorphs	—	+	—	+	—	++	+	—	—
XI	4	++ Lymphocytes ++ Polymorphs + Eosinophils	+	++	+	++	+	—	+	+	—
XII (Operative)	2	+ Lymphocytes + Polymorphs	++	+	+++	—	—	—	—	—	—
XIV	1.5	++ Lymphocytes + Polymorphs + Eosinophils	—	+	+	+	++	++	++	+	—
XV	2	+ Lymphocytes	—	—	+++	+	+	—	+	+	—

¹ The findings have been graded on an arbitrary system in which "—" represents a normal finding and "+", "++", "+++" represent increasing degrees of abnormality.

sinusoids around degenerating cells, and mitotic figures in these foci provided evidence of regeneration (Figure VII). Multinucleated cells were conspicuous in some specimens (Figure VIII).

The histological appearances thus varied in degree from case to case (Table II), but certain features were more or less constant. In the portal tracts there was a mild to moderate increase of fibroblasts, polymorphonuclear leucocytes and lymphocytes, without appreciable bile ductule proliferation; the parenchymal cells showed evidence of bile retention in the form of bile thrombi and intracytoplasmic granules, usually more marked in the centrilobular areas, together with patchy necrosis.

It should be noted that this fibroblastic activity occurring under the stimulus of acute liver injury rarely progresses to the formation of mature collagen. This was not present in biopsies obtained three months after the onset of jaundice. Portal fibrosis was found in Case IV at autopsy four years after the episode of cholestasis, but this patient was an alcoholic in whom nutritional factors were also operative. No fibrosis was found at autopsy in Case V.

Diagnostic Laparotomy.

Ten of the fifteen patients underwent laparotomy. In two initially admitted to surgical wards (Cases IX and XII) this preceded medical consultation; in another (Case VIII) who possibly shared his physician's anxiety, it was necessitated by the perforation of a duodenal ulcer after a diagnosis of acute cholestatic syndrome had been made, and conservative management decided upon. In the remaining seven patients laparotomy was advised as a diagnostic measure; six were in the first nine examined by us.

The operative findings were similar in all. The liver was enlarged, firm to palpation and green in colour. The capsule showed a finely nodular appearance. The gall-bladder and bile ducts were collapsed; when they were opened "white bile" was obtained. Gall-stones were absent in all instances. In two patients (Cases IV and V) free bile-stained fluid was present within the peritoneal cavity, and in a third peritonitis had followed the perforation of a chronic duodenal ulcer. In all cases the pancreas and other viscera showed no macroscopic abnormality.

Operative procedures varied. In Case XI cholecystectomy was performed. In every case the external biliary tree was explored and found normal, this being confirmed by direct cholangiography in Cases II and III. The common bile duct was drained in three cases and a wedge-biopsy of the liver obtained in all except Cases VIII and XV.

The patients withstood operation well. Only in Case V was there subsequent clinical deterioration. This case is discussed fully below. The relative tolerance of patients with acute cholestasis to surgery has been noted previously by several workers (Watson and Hoffbauer, 1946; Björneboe, Iversen and Trautner, 1952; Summerskill and Jones, 1958). Indeed in some instances exploration and drainage of the common bile duct has appeared to initiate recovery. Because of this, McSwain *et alii* (1958) and Strauss *et alii* (1959) consider that laparotomy and external biliary drainage are indicated in patients with prolonged jaundice from subacute or cholangiolitic hepatitis, and that surgical intervention produces rapid improvement and lessening of jaundice. This question must be regarded as highly controversial. Our experience is that laparotomy is indicated only as a diagnostic measure in the acute cholestatic syndrome, and that medical management leads to complete recovery in the majority of cases.

The anaesthetic agents used have varied, but there has been no evidence of liver damage from this cause in our patients.

Diagnosis.

The diagnosis of the acute cholestatic syndrome was thus made at very different stages in the disease in different patients. Acute non-obstructive jaundice was

diagnosed clinically in nine of the 15 patients. When our experience of the disease was not great, reliance was placed on negative flocculation test results to an extent that the initial diagnosis was sustained only after considerable further investigation, including liver biopsy and laparotomy. Study of more recent cases shows that, correctly interpreted, biochemical investigations are of great value in the diagnosis of the acute cholestatic syndrome. The characteristic picture is of a moderate or large increase in the serum bilirubin level with negative flocculation test results, but without any large elevation of the serum alkaline phosphatase level. There may or may not be a slight increase in the serum globulin level, but in only two of our cases did this reach 4.0 grammes per 100 ml. If these findings occur in conjunction with an increased SGOT level, a presumptive diagnosis may be made on biochemical grounds with some confidence. In this emphasis on the value of biochemical findings we differ from Shorter *et alii* (1959). Goldstein *et alii* (1959) also report high SGOT levels in 11 patients with cholangiolitic hepatitis.

The diagnostic problem presented by the liver biopsies in these cases is the distinction between jaundice from extrahepatic obstruction and that from parenchymatous liver disease. Cholestasis and hepatic cell degeneration occur in both types of jaundice, although in general the accent is on cholestasis in extrahepatic obstruction and on hepatic cell damage in parenchymatous disease. If bile thrombi are large and plentiful, and bile lakes and microcalculi can be found, the evidence for mechanical obstruction is strong; but because these changes cannot always be found in the limited amount of tissue provided by a liver biopsy, the absence of one or more of them does not exclude mechanical obstruction. Points we have found useful in differentiating between the two types of jaundice are those indicated by Dubin (1956), who found that in obstructive jaundice, focal necrosis tended to be limited to the centrilobular areas of bile stasis, while in primary cholestatic hepatitis the necrosis occurred haphazardly in the lobule and bore no constant relationship to the bile plugs. Bile plugs also tended to be fewer and smaller than in external biliary obstruction.

We have found liver biopsy to be a useful, but not infallible, aid in the diagnosis of acute cholestasis, and its value has increased with increased experience of both the clinician and the pathologist. Thus, an histological diagnosis of biliary obstruction led to laparotomy in our first three cases, although in Case I only after a second biopsy five weeks later. Since this time either the diagnosis has been made without laparotomy (Cases VII, VIII, X, XI, XIII and XIV), or laparotomy has been performed without a preliminary needle biopsy (Cases IV, V, VI, IX and XII). In Cases IV, V, and VI this was in part due to an unusually high alkaline phosphatase level; in Cases IX and XII the patients were referred directly to a surgical ward and were examined in consultation only after laparotomy showed no surgical cause for the jaundice. Only in Case XV was an incorrect preoperative diagnosis made after liver biopsy.

Our present position is that a diagnosis of the acute cholestatic syndrome may, in the great majority of cases, be made firmly on clinical and biochemical data, supplemented in some instances by liver biopsy. Laparotomy is rarely necessary to substantiate this diagnosis. We have no experience of the use of steroid therapy as a diagnostic measure in this situation.

Course of the Disease.

As has been mentioned, the course of the disease differed greatly in the two sexes, and for this reason they are conveniently considered separately.

In the female patients the course was generally benign. After a typical onset usually in relation to or following pregnancy, a moderate degree of jaundice developed and lasted in five of the six cases for less than two months. Constitutional upset was not great,

only one patient having significant weight loss. Biochemical tests showed an increase in the serum bilirubin level and a slight hyperglobulinemia. Diagnosis presented few difficulties, and laparotomy was performed upon only one of the five patients admitted to a medical ward.

These features are best illustrated by a typical case report, in which a diagnosis of homologous serum jaundice was made.

CASE XIV.—A female patient, aged 33 years, was admitted to hospital on January 31, 1959. Four months previously, after the birth of her eighth child, she had a post-partum hemorrhage and received a transfusion of two pints of blood. After this she did not regain her usual health, but noted no specific other symptoms. Her weight remained constant and she had no dyspepsia or alteration of bowel habit. She knew of no contact with a jaundiced person. Two weeks before admission to hospital she developed weakness, and this was followed by epigastric discomfort and anorexia. Jaundice and dark urine were first observed on the day of her referral to hospital.

On examination she was afebrile and moderately jaundiced, with liver palpable 3 cm. below the right costal margin and a palpable spleen.

A diagnosis was made of homologous serum hepatitis. However, a negative result was obtained from the thymol turbidity test and the serum alkaline phosphatase level was 34 King-Armstrong units, although the SGOT level was 368 units. It was therefore decided to perform liver biopsy, which was done on February 6, the seventh day of the jaundice. This showed unequivocal evidence of active hepatitis in the phase of early regeneration. The lobular architecture was well preserved, but many parenchymal cells showed degenerative changes with frequent hydropic degeneration and eosinophilic necrosis, as well as frequent mitoses and double cell columns indicating parenchymal regeneration. There were occasional bile thrombi and bile-stained polygonal cells (Figure V). A diffuse infiltration with polymorphonuclear leucocytes, lymphocytes and plasma cells was present in the sinusoids and portal tracts.

Conservative management, without steroid therapy, was followed by clinical and biochemical recovery over the ensuing four weeks (Figure IX). A subsequent intravenous cholecystogram has demonstrated a normal gall-bladder and biliary tree. The patient has remained well since.

The duration of jaundice varied. In five of the six female patients it was relatively short—four, five, six, eight and nine weeks respectively—and in all these cases clinical and biochemical recovery was complete. As is not unusual in acute hepatitis, recovery in some cases was followed by a variable period of vague malaise and ill-health, which resolved gradually over a period of weeks or months. The length of follow-up of these patients has ranged from one to 15 months. The sixth female patient (Case XIII) presented a slightly more difficult problem. She first was noted to be icteric in the fifth month of pregnancy and remained so during pregnancy and after delivery. This jaundice was unaffected by steroid therapy. However, she was lost to follow-up one month after delivery, and her subsequent history and final diagnosis are unknown.

A point of some importance is that both patients (Cases XII and XIII) who developed the acute cholestatic syndrome during pregnancy had normal labours, and in both the infant was alive and unaffected. Neither of our patients has again become pregnant, but Svanbourg and Ohlsson (1959) suggest that further pregnancies may be attended by further jaundice. This is not progressive and the ultimate prognosis is excellent.

In the nine male patients the course of the disease was more severe; not only was the duration of the jaundice greater, but the only case in which death occurred in the acute stage was in a male patient. These patients were in general older, their ages ranging from 37 to 64 years. The onset of the disease was gradual, but the prodromal symptoms were generally more intense. Loss of weight was a frequent symptom; five lost a stone or more and two others slightly less than this, although the diet prior to illness had been good in all

cases. Anorexia, nausea and vomiting were marked in eight of the nine patients. Seven of them commented upon the itching of the skin. Three of the eight gave a clear history of a hepatitis contact, and one had received a recent blood transfusion.

The greater diagnostic difficulties presented by the acute cholestatic syndrome in the male are reflected in two features: an initial diagnosis of acute parenchymal jaundice was made in only three, and diagnostic laparotomy was advised in six of our eight cases.

Jaundice was generally deeper and more prolonged than in the females. The serum bilirubin exceeded 20 mg. per 100 ml. at some stage of the disease in four cases, and the average duration of jaundice was just under three months.

In seven patients recovery, if slow, was steady and progressive, although the disappearance of jaundice was often followed by a prolonged period of lassitude and

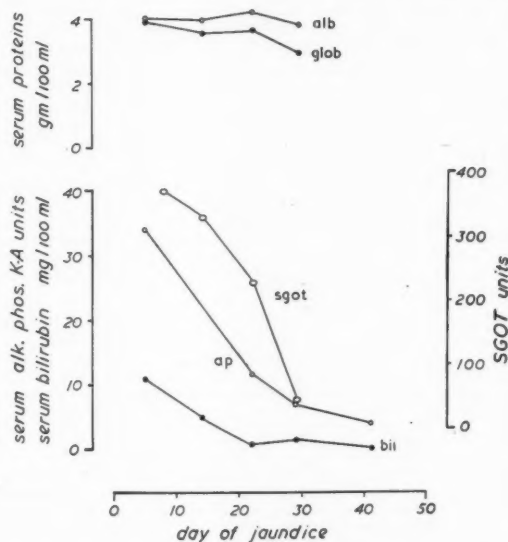


FIGURE IX.

Serial biochemical findings in a female patient, aged 33 years, with acute cholestasis probably caused by hepatitis B virus infection (Case XIII).

debility, and full rehabilitation was delayed. Of the other two, one died in the acute stage of hepato-renal failure, and the other developed acute hemolytic anemia during his convalescence. Both these cases are of sufficient interest to describe in some detail.

CASE V.—A male patient, aged 46 years, was admitted to hospital on September 17, 1953, for the investigation of jaundice. Six weeks previously he had become anorexic. Jaundice appeared a week later and was associated with choloria and pallor of the stools. There was no history of hepatitis contact or exposure to hepatotoxins. He was treated at home with bed rest and a fat-free diet, but lost weight steadily and the degree of jaundice, although fluctuating, slowly increased so that he was referred to hospital.

On examination he was wasted and deeply jaundiced. There was a slight pyrexia of 99° F. The liver was firm and palpable 3 cm. below the right costal margin and free fluid was present in the peritoneal cavity. The stigmata of cirrhosis were not present. The urine was of low specific gravity, but did not contain excess protein. Investigations showed the picture of obstructive jaundice. The serum bilirubin level was 25 mg. per 100 ml., the alkaline phosphatase level 70 King-Armstrong units, all flocculation test gave negative results and the serum protein pattern was normal. Occult blood was present in the faeces. The blood-urea level was 120 mg. per 100 ml. Other investigations were not helpful.

The initial diagnosis in this case was that of cirrhosis of the liver, but the biochemical profile and the occult blood raised sufficient suspicion of carcinoma for laparotomy to be undertaken. At operation one week after admission, free bile-stained fluid was found in the peritoneal cavity, the liver was enlarged and deeply bile-stained and the gall-bladder and bile ducts were collapsed. There was no evidence of cholelithiasis or carcinoma. A liver biopsy was taken and the common duct was drained. After operation the jaundice increased and no bile drained from the T-tube, while the alkaline phosphatase level rose to 85 King-Armstrong units. Although a good urinary output was maintained and the patient's blood pressure did not fall, his blood-urea level steadily rose to 309 mg. per 100 ml., on the eighth day after operation. He died two days later in acute central and peripheral circulatory failure.

Post-mortem examination confirmed the operative findings. Extensive dissection revealed no external biliary obstruction and the biliary tree was normal. There was slight pancreatic atrophy and fibrosis. The kidneys showed "toxic bile nephrosis". Sections from the liver showed extensive bile retention with minimal parenchymal cell damage. The final diagnosis was therefore of the acute idiopathic cholestatic syndrome with hepato-renal failure.

This case emphasizes the association of the acute cholestatic syndrome with renal failure stressed by Dible, McMichael and Sherlock (1947) and by Palmer (1958).

CASE IV.—A male patient, aged 61 years, was admitted to hospital on March 23, 1954, for investigation of jaundice. He stated that he had had transient jaundice of unknown nature one year previously. Three weeks before admission to hospital he developed painless progressive jaundice with dark urine and pale faeces. A week later this was followed by nausea, vomiting and epigastric pain, occurring chiefly before meals and worse in the morning. His diet had been poor and he was a mild alcoholic. He had lost five pounds in weight.

On examination he was febrile (temperature 100.4° F.) and jaundiced. The liver edge was palpable 3 cm. below the right costal margin, but the spleen was impalpable and stigmata of chronic liver disease were not present. The diagnostic difficulty in this patient led to considerable laboratory investigation. Hyperbilirubinaemia and an increased alkaline phosphatase level, with negative flocculation test results suggested obstructive jaundice. The serum albumin level was 3.1 grammes per 100 ml.; the serum globulin level was 2.9 grammes per 100 ml.; the haemoglobin value was 8.4 grammes per 100 ml.; the white-cell count was 10,000 per c.mm.; the blood-urea level was 27 mg. per 100 ml.; the Wassermann reaction was negative; the Coombs' test gave a negative result; the Casoni test gave a negative result; and the faecal stercobilin value was 14 mg.%. Radiological studies, including a barium-meal examination, revealed no abnormality, although a histamine-fast achlorhydria was present. Bone-marrow biopsy showed erythroid hyperplasia and occasional large plasma cells with vacuolated cytoplasm containing small basophil inclusions.

After preliminary blood transfusion laparotomy was performed on April 1. Clear, bile-stained fluid was found in the peritoneal cavity, the liver was enlarged, green, and finely nodular and the gall-bladder and bile ducts were collapsed and showed no abnormality. An extensive search revealed no cause for, or evidence of, external biliary obstruction. A liver biopsy was taken, but no other operative procedure performed.

After operation there was considerable oozing of ascitic fluid from the operation wound, and this fistula did not close for four weeks. The jaundice faded steadily and the alkaline phosphatase level returned to normal. However, the patient developed a progressive anaemia despite repeated blood transfusion and, as there was no evidence of blood loss and an active bone marrow, further investigation was undertaken. Two weeks after operation the direct Coombs test was found to give a strongly positive result and the faecal stercobilin had risen to 262 mg.%. Hemolysins and auto- and iso-agglutinins could not be demonstrated and examination for lupus erythematosus cells yielded negative results. Cortisone therapy was begun in an initial dose of 150 mg. daily, and a week later the Coombs test gave a negative result, while the haemoglobin level was maintained. The patient was discharged from hospital on May 16 after cessation of the steroid therapy.

He was examined again in the follow-up clinic on September 29, when he was well and had regained his weight. There was no enlargement of the liver or the spleen, and no ascites. All the liver function tests gave

normal results. His haemoglobin value was 13.1 grammes per 100 ml. The Coombs test gave a negative result, but hemolysins were demonstrated in his serum for the first time.

His final admission to hospital was on March 29, 1958, with massive upper gastro-intestinal hemorrhage, from which he died within an hour of admission. Post-mortem examination showed "post-necrotic" cirrhosis, with splenomegaly and oesophageal varices which appeared to be the source of bleeding.

This patient presents several unsolved problems. It would seem probable in retrospect that he had an intermittent auto-immune haemolytic anaemia which was the cause of his two episodes of jaundice, the second of which progressed to an acute cholestatic syndrome. The relative roles of time, surgery and steroids in his recovery from this are uncertain. The absence of mechanical obstruction of the bile ducts is supported by the clinical picture and the operative findings. The development of the cirrhosis shown at autopsy would seem to have been due to alcoholism and repeated haemolytic episodes, and possibly to an auto-immune mechanism of the type operative in some other forms of chronic hepatitis (Joske and King, 1955; MacKay *et alii*, 1956) rather than to his cholestatic syndrome. The initial biopsy taken at operation showed considerable fibrosis and his cirrhosis was of portal rather than biliary type. However, it is not possible to be sure of this, and it well may be that cholestasis was one component in a multifactorial situation. The stimulation of extrahepatic obstruction by liver disease in chronic alcoholism has been stressed by Phillips and Davidson (1957).

Our management of these cases has generally been conservative. When the diagnosis is established, bed rest and dietetic measures alone have produced recovery in all cases except IV and V. In Case IV recovery occurred from the acute episode, although steroids were used to control the hemolytic anaemia; after this the patient was seen only once before his terminal admission three years later. Case V has already been discussed; in the light of our present knowledge we would now probably use steroids in this situation. It should be mentioned that we consider active chronic hepatitis and lupoid hepatitis are indications for prolonged steroid therapy.

Discussion.

These patients and others reported in the literature present a definite clinical and biochemical picture which is capable of recognition in most instances. It is of diverse aetiology, and causative factors identified include hepatitis viruses A and B, pregnancy and drugs such as arsphenamine, methyl testosterone and chlorpromazine. Because of this multiple aetiology, this syndrome is best regarded not as a disease *stricto sensu*, but as an atypical pattern of hepatic reaction to different agents. Nor is it probable that these different agents produce the same picture by the same pathological mechanism.

In viral hepatitis there is little doubt that the primary lesion is parenchymal cell damage. This is shown by the biochemical and histological findings in typical cases. It probably also applies to the cholestatic syndrome when this is the result of acute viral hepatitis, although in the absence of a specific diagnostic test this must depend on statistical and epidemiological evidence. Of the present cases, six were probably due to viral hepatitis, and except in Case XV, SGOT levels were higher than those found in external biliary obstruction. The initial viral infection was therefore not severe, a suggestion borne out by the mild clinical picture and negative flocculation test results. Indeed, only with slight parenchymal damage would bile continue to reach the canaliculi; severe hepatitis may be accompanied by acholic stools (Steigmann and Popper, 1943). This initially mild hepatitis is then converted to a more prolonged cholestatic picture by the formation of bile plugs and microcalculi in the canaliculi by some other factor, the nature of which is considered below.

Two other theories of this process have been advanced but appear less probable in the present state of knowledge.

It has been suggested that in cholangiolitic hepatitis there may be direct involvement of the bile ductules rather than the parenchymal cells by virus action. This does not explain the results of enzymatic tests in this condition, especially the slight elevation of serum alkaline phosphatase levels and the considerable increase in SGOT levels, nor is it fully in accord with the histological findings. It has also been suggested that this variant of viral hepatitis may be due to an unusual strain of virus rather than an unusual pattern of host response. There is, in fact, some evidence that hepatitis B infection is more likely to result in this picture than is hepatitis A infection (Turner *et alii*, 1944), but generally the epidemiological evidence does not support the theory. However, its accurate investigation is not currently possible.

In cholestasis arising from drugs different pathogenetic mechanisms operate. Jaundice from arsphenamine and chlorpromazine probably involves a hypersensitivity mechanism. This is suggested by the time relation between the administration of the drug and the onset of jaundice, the frequent association with skin lesions and eosinophilia, the histology of the liver changes, and the response to steroids which occurs even if the drug administration is continued (Trethowan and Shand, 1958). The earliest and characteristic biochemical finding of these patients is an increased serum alkaline phosphatase level. In general terms such increases are associated with lesions causing obstruction, irritation or proliferation of the bile ducts, rather than with parenchymal cell damage. It is possible, therefore, that in cholestasis complicating drug hypersensitivity, the primary lesion may well be an antigen-antibody mechanism occurring distal to the parenchymal cells, although Burton *et alii* (1958) found that chlorpromazine affected diphosphopyridine nucleotide synthesis in the liver. Drugs causing direct parenchymal damage, such as carbon tetrachloride and iproniazid, do not produce the cholestatic syndrome, but a syndrome indistinguishable from viral hepatitis (Rosenblum *et alii*, 1960).

Cholestasis due to methyl testosterone and norethandrolone is not associated with evidence of parenchymal cell damage or hypersensitivity mechanisms, while we have observed that it occurred in a patient who was already receiving steroid therapy. The mechanism here may be an alteration in the physico-chemical character of the bile resulting from excretion by the liver of the steroid, and leading to precipitation of thrombi. Both these steroids possess an alkyl group at C17 (Shaw and Gold, 1960).

In cholestasis related to pregnancy and the recurrent jaundice described by Svanbourg (1954), a similar pathogenesis is possible. Studies of liver function during pregnancy have yielded variable results (Lichtman, 1953; Thorling, 1955), but there is little clinical or laboratory evidence of parenchymal cell damage in normal pregnancy. However, there is some evidence that bile stasis is frequent and excretory function impaired, as shown by bilirubin, bromsulphthalein and hippuric acid excretion studies, and by oral cholecystography. In addition, late pregnancy is accompanied by hypercholesterolemia and alterations in serum lipo-protein fractions. It is therefore possible that cholestasis of pregnancy has a similar origin to that following administration of methyl testosterone, in a change in the physical state of the bile resulting from altered steroid excretion, accompanied by smooth muscle relaxation and a slowing of the bile flow. Such a mechanism may also account for the association of cholelithiasis and pregnancy.

The cases of acute cholestasis in the absence of these factors present an unsolved problem. They are usually assumed to be due to viral hepatitis and this may be true in some patients. However, it does not explain recurrent cholestasis, such as was observed by Summerskill and Walshe (1959).

The chronicity of the cholestatic syndromes also presents problems. In some instances (such as Case IV of the present series) an auto-immune mechanism may be operative. MacKay (1958) has described a patient

with primary biliary cirrhosis showing a high titre of auto-antibody, in whom remission followed steroid therapy. A more promising approach is based upon the increasing evidence that bile itself is toxic (Cameron, 1958), and that bile stasis, however caused, results by chemical means in liver damage which may progress unless the stasis is relieved. Reichel and his colleagues (1960) have demonstrated abnormalities of microvilli by electron microscopy in this situation, but it is uncertain whether these are the primary change or secondary structural changes.

A further factor, so far little investigated, is that bilirubin excretion may vary from person to person. The failure of glucuronidation in Gilbert's disease and the Crigler-Najjar (1952) syndrome is now generally accepted, and the types of patient described by Svanbourg (1954), Summerskill and Walshe (1959) and Haverback and Wirtschafter (1960) may also represent clinical manifestations of anomalous bilirubin excretion. This would appear the most profitable field for further study.

Summary.

The literature concerning cholangiolitic hepatitis and related syndromes is reviewed and 15 further cases of the acute cholestatic syndrome not resulting from drugs are reported. These comprised nine males and six females aged from 23 to 64 years. The clinical picture of the disease resembled that of viral hepatitis with jaundice and liver enlargement, but in all cases biochemical investigation showed normal serum proteins, negative flocculation test results and slight to moderate increases in the serum alkaline phosphatase level. The SGOT level was increased to over 200 units in four of six cases in which it was estimated. Liver biopsies showed bile retention and fibroblastic proliferation and cellular infiltration of the portal tracts, with patchy necrosis of parenchymal cells. Nine of the 15 patients underwent diagnostic laparotomy, but it is thought that with increased definition and recognition of this disease surgery will be required less often for diagnosis in the future. The course of the disease was more severe in males than in females, in that jaundice was deeper and more prolonged in the males, and that two males died, one in the acute stage of hepato-renal failure and one four years later of hepatic cirrhosis. The pathogenesis of the cholestatic syndrome is discussed and it is considered to be a pattern of hepatic reaction to injury which may be evoked by different agents.

Acknowledgements.

Our thanks are due to Dr. Ian Wood, of the Walter and Eliza Hall Institute, Royal Melbourne Hospital, for permission to report Cases I to V (the patients were examined by us while under his care), and to our colleagues at the Royal Perth Hospital for allowing us to study their patients and for their continued help in this study. The photomicrographs were prepared by Mr. H. Upeniecks, of the University of Western Australia.

References.

- AHRENS, E. H. JUN., PAYNE, M. A., KUNKEL, H. G., EISENMENGER, W. J., and BLONDHEIM, S. H. (1950), "Primary Biliary Cirrhosis", *Medicine (Baltimore)*, 29: 299.
- AZIMA, H., and OGLE, W. (1954), "Effects of Largactil in Mental Syndromes", *Canad. med. Ass. J.*, 71: 116.
- BJØRNEBOE, M., IVERSEN, P., and TRAUTNER, K. (1952), "Obstructive Jaundice with Negative Findings at Operation", *Acta med. scand.*, 141: 249.
- BURTON, R. M., KAPLAN, N. O., GOLDIN, A., LEITENBERG, M., HUMPHREYS, S. R., and SODD, M. A. (1953), "Effect of Reserpine and Promazine on Diphosphopyridine Nucleotide Synthesis in Liver", *Science*, 127: 30.
- CABAUD, F., LEEFER, R., and WROBLEWSKI, F. (1956), "Colorimetric Measurement of Serum Glutamic Oxaloacetic Transaminase", *Amer. J. clin. Path.*, 26: 1101.
- CAMERON, G. R. (1958), "Some Problems of Biliary Cirrhosis", *Brit. med. J.*, 1: 535.
- CHALMERS, T. C., GILL, R. J., JERNIGAN, T. P., SVET, F. A., JORDAN, R. S., WALSTEIN, S. S., and KNOWLTON, M. (1956), "Evaluation of a Four-day ACTH Test in the Differential Diagnosis of Jaundice", *Gastroenterology*, 30: 894.

- CRIGLER, J. F. JUN., and NAJJAR, V. A. (1952), "Congenital Familial Non-hemolytic Jaundice with Kernicterus", *Pediatrics*, 10: 169.
- DIBLE, J. H., MCMICHAEL, J., and SHERLOCK, S. (1947), "Chronic Retention Jaundice in Elderly Patients", *Gastroenterology*, 9: 736.
- DUBIN, I. N. (1956), "Cholestatic Hepatitis (Primary Pericholangitis: Cholangiolitic Hepatitis)", *Bull. N.Y. Acad. Med.*, 32: 396.
- DUBIN, I. N., and JOHNSON, F. B. (1954), "Chronic Idiopathic Jaundice with Unidentified Pigment in Liver Cells", *Medicine (Baltimore)*, 33: 155.
- ELIAKIM, M., and RACHMILSWITZ, M. (1956), "Cholangiolitic Manifestations in Virus Hepatitis", *Gastroenterology*, 31: 369.
- FOULK, W. T., BUTT, H. R., OWEN, C. A. JUN., WHITCOMBE, F. F. JUN., MASON, H. L. (1959), "Constitutional Hepatic Dysfunction (Gilbert's Disease): its Natural History and Related Syndromes", *Medicine (Baltimore)*, 38: 25.
- GALL, E. A., and BRAUNSTEIN, H. (1955), "Hepatitis with Manifestations Simulating Bile Duct Obstruction", *Amer. J. clin. Path.*, 25: 1113.
- GOLDBRABER, M. B., and KIRSNER, J. B. (1959), "The Use of Adrenal Steroids in Subacute and Chronic Cholangiolitic Hepatitis", *A.M.A. Arch. intern. Med.*, 103: 354.
- GOLDSTEIN, F., SELIGSON, D., and BOCKUS, H. L. (1959), "Serum Glutamic Oxaloacetic Transaminase and Iron in the Differential Diagnosis of Jaundice", *Gastroenterology*, 36: 487.
- HANGER, F. M. JUN., and GUTMAN, A. B. (1940), "Postarphenamine Jaundice", *J. Amer. med. Ass.*, 115: 263.
- HAVERBACK, B. J., and WIRTSCHAFTER, S. K. (1960), "Familial Non-hemolytic Jaundice with Normal Liver Histology and Conjugated Bilirubin", *New Engl. J. Med.*, 262: 113.
- JOHNSON, H. C. JUN., and DOENIGES, J. P. (1956), "Intrahepatic Obstructive Jaundice (Primary Cholestasis), a Clinicopathologic Syndrome of Varied Etiology: a Review with Observations of the Use of Corticotrophin as a Diagnostic Tool", *Ann. intern. Med.*, 44: 589.
- JOSKE, R. A., and KING, W. E. (1955), "The 'L.E.-Cell' Phenomenon in Active Chronic Viral Hepatitis", *The Lancet*, 2: 477.
- KATE, R. DUCCI, H., and ALBESANDRI, H. (1957), "Influence of Cortisone and Prednisolone on Hyperbilirubinemia", *J. clin. Invest.*, 36: 1370.
- KLATSKIN, G. (1956), "Toxic Hepatitis", in "Diseases of the Liver", Edited by L. Schiff, Philadelphia: 328.
- LAST, P. M. (1957), "The Treatment of Active Chronic Infectious Hepatitis with ACTH (Corticotrophin) and Cortisone", *Med. J. Aust.*, 1: 672.
- LATNER, A. L., and SMITH, A. J. (1958), "Serum Transaminase: Alkaline Phosphatase Ratio in Differential Diagnosis of Jaundice", *The Lancet*, 2: 915.
- LICHTMAN, S. S. (1953), "The Liver in Pregnancy, Diseases of the Liver, Gallbladder and Bile Ducts", Philadelphia, 2: 940.
- LIPSCHUTZ, E. W., and CAPSON, D. (1955), "Cholangiolitic Hepatitis, with Special Reference to its Physiopathologic Concept, Diagnosis and Therapy", *Ann. intern. Med.*, 43: 1037.
- MACKEY, I. R. (1958), "Primary Biliary Cirrhosis Showing a High Titer of Autoantibody", *New Engl. J. Med.*, 258: 185.
- MACKEY, I. R., TAFT, L. I., and COWLING, D. C. (1956), "Lupoid Hepatitis", *The Lancet*, 2: 1323.
- MCSWAIN, B., HERRINGTON, J. L. JUN., EDWARDS, W. H., SAWYERS, J. L., and CATE, W. R. JUN. (1958), "Intrahepatic Cholangiolitic Hepatitis: its Surgical Significance", *Ann. Surg.*, 147: 305.
- OVERHOLT, E. L., and HARDIN, E. B. (1959), "Cholangiolitic Hepatitis. Clinical-pathologic Studies and Response to Steroid Therapy in Four Cases", *A.M.A. Arch. intern. Med.*, 103: 859.
- PALMER, E. D. (1958), "Anuria and Cholangiolitic Hepatitis", *Amer. J. dig. Dis.*, 3: 469.
- PHILLIPS, G. B., and DAVIDSON, C. S. (1957), "Liver Disease of the Chronic Alcoholic Stimulating Extrahepatic Biliary Obstruction", *Gastroenterology*, 33: 236.
- POPPER, H., and SCHAFFNER, F. (1959), "Pathology of Jaundice Resulting from Intrahepatic Cholestasis", *J. Amer. med. Ass.*, 169: 1447.
- POPPER, H., and SCANTO, P. B. (1956), "Intrahepatic Cholestasis ('Cholangiolitis')", *Gastroenterology*, 31: 683.
- REICHEL, J., GOLDBERG, S. B., ELLENBERG, M., and SCHAFFNER, F. (1960), "Intrahepatic Cholestasis Following Administration of Chlorpromazine", *Amer. J. Med.*, 28: 554.
- ROSENBLUM, L. E., KORN, R. J., and ZIMMERMAN, H. J. (1960), "Hepatocellular Jaundice as a Complication of Iproniazid Therapy", *A.M.A. Arch. intern. Med.*, 105: 583.
- SAINT, E. G. (1952), "Infectious Hepatitis in Old Age Groups", *Med. J. Aust.*, 2: 613.
- SAINT, E. G., KING, W. E., JOSKE, R. A., and FINCKH, E. S. (1953), "The Course of Infectious Hepatitis with Special Reference to Prognosis and the Chronic Stage", *Aust. Ann. Med.*, 2: 113.
- SEBROV, V. M., GIGGS, B., PLOUGH, I. C., and MENDEL, W. (1954), "ACTH Therapy in Acute Viral Hepatitis", *J. Lab. clin. Med.*, 43: 48.
- SHALDON, S., and SHERLOCK, S. (1957), "Virus Hepatitis with Features of Prolonged Bile Retention", *Brit. med. J.*, 2: 734.
- SHAW, R. K., and GOLD, G. L. (1960), "Jaundice Associated with Norethandrolone ('Nilevar') Therapy", *Ann. intern. Med.*, 52: 428.
- SHORTER, R. G., PATON, A., and PINNIGER, J. L. (1959), "Hepatic Jaundice", *Quart. J. Med.*, 28: 43.
- SOLIM, J. H., and OLSEN, A. (1953), "The Course of Icterus Index and Prothrombin Value During Corticotrophin Treatment of Acute Hepatitis and Obstructive Jaundice", *Acta med. scand.*, 146: 231.
- SPRING, H., and NELSON, R. S. (1954), "Persistent Non-hemolytic Hyperbilirubinemia Associated with Lipochrome-like Pigment in Liver Cells", *Ann. intern. Med.*, 41: 952.
- STRAUSS, A. A., STRAUSS, S. F., SCHWARTZ, A. H., TENNENBAUM, W. J., KRAM, D. D., and SILVER, J. M. (1959), "Liver Decompression by Drainage of the Common Bile Duct in Subacute and Chronic Jaundice", *Amer. J. Surg.*, 97: 137.
- STREIGMAN, F., and POPPER, H. (1943), "Intrahepatic Obstructive Jaundice", *Gastroenterology*, 1: 645.
- SUMMERSKILL, W. H. J., and JONES, F. A. (1958), "Corticotrophin and Steroids in the Diagnosis and Management of 'Obstructive' Jaundice", *Brit. med. J.*, 2: 1499.
- SUMMERSKILL, W. H. J., and WALSH, J. M. (1959), "Benign Recurrent Intrahepatic 'Obstructive' Jaundice", *The Lancet*, 2: 686.
- SVANBOURG, A. (1954), "A Study of Recurrent Jaundice in Pregnancy", *Acta obst. Gynec. scand.*, 33: 433.
- SVANBOURG, A., and OHLSSON, S. (1959), "Recurrent Jaundice of Pregnancy", *Amer. J. Med.*, 27: 40.
- THORLING, L. (1955), "Jaundice in Pregnancy", *Acta med. scand.*, Supplement: 302.
- TRETHOWAN, W. H., and SHAND, J. W. (1958), "Resolution of Chlorpromazine Jaundice Without Withdrawal of the Drug", *Med. J. Aust.*, 1: 568.
- TURNER, R. H., SNAVELY, J. R., GROSSMAN, E. B., BUCHANAN, R. N., and POSTER, S. O. (1944), "Some Clinical Studies of Acute Hepatitis Occurring in Soldiers after Inoculation with Yellow Fever Vaccine: with Special Consideration of Severe Attacks", *Ann. intern. Med.*, 20: 193.
- WATSON, C. J., and HOFFBAUER, F. W. (1946), "The Problem of Prolonged Hepatitis with Particular Reference to the Cholangiolitic Type and to the Development of Cholangiolitic Cirrhosis of the Liver", *Ann. intern. Med.*, 25: 195.
- WERNER, S. C., HANGER, F. M., and KARLBERG, R. A. (1950), "Jaundice During Methyl Testosterone Therapy", *Amer. J. Med.*, 8: 325.
- ZATUCHNI, J., and MILLER, G. (1954), "Jaundice During Chlorpromazine Therapy", *New Engl. J. Med.*, 251: 1002.

Legends to Illustrations.

FIGURE I.—Portal tract infiltrated by fibroblasts and lymphocytes (Case X). $\times 640$. Eosin and hematoxylin stain.

FIGURE II.—Polymorphonuclear leucocytes, fibroblasts and lymphocytes amongst peripheral parenchymal cells (Case VIII). $\times 640$. Hematoxylin and eosin stain. FIGURE III.—Conspicuous biliary thrombi in centrilobular zone (Case VI). $\times 640$. (Kodak Wratten 38A Filter.) Hematoxylin and eosin stain. FIGURE IV.—Degenerating parenchymal cells, with abundant intracytoplasmic bile granules, near central vein (Case VIII). $\times 640$. Hematoxylin and eosin stain.

FIGURE V.—Anisocytosis of parenchymal cells, irregular liver plates, and multinucleated cells (Case XII). Hematoxylin and eosin stain. $\times 640$. FIGURE VI.—Dilated blood filled sinusoids where parenchymal cells have disappeared. Ballooned and shrunken cells present (Case X). Hematoxylin and eosin stain. $\times 640$. FIGURE VII.—A mitotic figure is shown centrally. In another area there are polymorphonuclear leucocytes aggregated around degenerating parenchymal cells (Case VIII). Hematoxylin and eosin stain. $\times 640$. FIGURE VIII.—Multinucleated parenchymal cells are seen adjacent to central vein (Case IX). Hematoxylin and eosin stain. $\times 640$.

THE MANAGEMENT OF TETANUS.

By B. S. CLIFTON,

Staff Anaesthetist, Royal Prince Alfred Hospital, Sydney.

THIS communication is a description of practical and certain theoretical aspects of the management of tetanus at Royal Prince Alfred Hospital. No doubt this management will require variation for certain patients and alterations in the light of future experience, but it is hoped that the description will be of interest to others treating this disease and of value to those meeting it for the first time. As tetanus is a disease requiring intensive care, many of the principles mentioned here have wider application in medicine and surgery. Table I shows a practical classification of tetanus, with respect to the severity and the management followed at Royal Prince Alfred Hospital at the present time.

The tetanus A pati constan Admis is idea for tet and a consist the cli him. medica of nur work i import sufficien tinuity special history next 24 the cor or by t in the of the surgica

On t painful of diall chlorpr weight. tetanus theatre followi into a l entry w by the movem The tetanus tracheo therapy of seco some d

The treatme implies ment, p without anaest process briskly chlorpr are of muscula Barbi acting c per kilo to six h mg. per forms a

* As 10 is neces per 2 ml

TABLE I.

Degree of Severity.	Incubation Period (Days.)	Period of Onset (Hours.)	Early Pyrexia.	Tracheostomy.	Intravenous Therapy.	Chlorpromazine Therapy.	Neuromuscular Blocking Agent.
Mild	14 to 21	Less than 48	No	Probably yes	Yes	Yes	No
Moderate	7 to 14	24 to 48	No	Yes	Yes	Probably no	Probably yes
Severe	Less than 7	Less than 24	Yes	Yes	Yes	No	Yes

The complexity and the intensity of the therapy of tetanus are a serious drain upon the staff of any hospital. A patient with moderately severe or severe disease needs constant attention 24 hours each day for four or five weeks. Admission to an intensive care ward within the hospital is ideal; but, failing this, a small unit designed especially for tetanus is effective. Such a unit exists at this hospital, and a special team controls its management. This team consists of four physicians, a staff anaesthetist, and either the clinical superintendent or a registrar appointed by him. The actual management is carried out by three medical officers on eight-hour shifts and as small a number of nurses as possible. A medical officer is not expected to work in this team for more than three weeks. The importance of restricting changes of personnel cannot be sufficiently emphasized, because only then can the continuity and effectiveness of therapy be guaranteed. A special cyclostyled form is placed in front of the patient's history to summarize the management intended for the next 24-hour period. Any alteration in this is effected by the completion of another form by the registrar in charge or by a senior member of the team. Invaluable assistance in the management of tetanus is provided by all branches of the Institute of Pathology and by the physiotherapy and surgical departments.

Preliminary Therapy.

On the patient's admission to hospital, rapid control of painful rigidity is obtained by the intramuscular injection of diallylbarbituric acid and the intravenous injection of chlorpromazine, each 1.5 to 2.0 mg. per kilogram of body weight. A subcutaneous test dose of 0.5 ml. of 1:50 anti-tetanus serum is given. An early visit to the operating theatre is necessary in all cases for one or more of the following procedures: (a) insertion of a plastic cannula into a large vein; (b) a tracheostomy; (c) excision of the entry wound. A decision on each of these points is made by the team before the visit to the theatres, so that useless movement of the patient is avoided.

The five principal considerations in the therapy of tetanus are as follows: (i) sedation and relaxation; (ii) tracheostomy; (iii) artificial respiration; (iv) intravenous therapy; (v) eradication of the disease; (vi) prevention of secondary infections. Each will now be discussed in some detail.

Sedation and Relaxation.

The sedation-relaxation regime is the sheet-anchor of treatment. It aims to control the tetanic process. Control implies sufficient relaxation to permit all phases of management, particularly physiotherapy and tracheal aspiration, without the precipitation of asphyxiating rigidity. Deep anaesthesia is avoided so that homeostatic and metabolic processes may remain active. Pupils are always small and briskly reactive to light. This means that agents such as chlorpromazine (Robson and Keele, 1956) and tubocurarine are of great value, because they specifically depress neuromuscular effector pathways.

Barbiturates are ideal sedatives. The moderately long-acting diallylbarbituric acid,¹ in a dosage of 20 to 30 mg. per kilogram per day, is given intramuscularly every four to six hours. A slow infusion of "Sodium Amytal", 20 to 30 mg. per kilogram per day, is effective, but not ideal, as it forms a precipitate with chlorpromazine. Soluble pheno-

barbitone given intramuscularly has such a prolonged action that gross accumulation may appear after several days (Goodman and Gilman, 1955). Sedation is continued for at least 21 to 28 days until muscle rigidity disappears.

Initially an attempt is made to control muscle rigidity with chlorpromazine, and this proves successful in all mild and some moderately severe cases. Beginning at a dosage of 0.5 mg. of chlorpromazine per kilogram per hour, the rate of intravenous administration is increased gradually to 1 mg. per kilogram per hour. If the latter does not result in rapid control of the tetanus, tubocurarine is started. Chlorpromazine is acid and highly irritant, so that prolonged high dosage necessitates the use of a "Polythene" catheter in a large vein to avoid extensive thrombosis of superficial veins. Intermittent administration by vein every two or three hours tends to prevent emergence of drug resistance.

The indications for the use of neuro-muscular blockade in the therapy of tetanus are: (a) an incubation period of certainly less than seven days; (b) a period of onset of less than 24 hours; (c) rapidly increasing severity of spasms despite the administration of 1 mg. of chlorpromazine per kilogram per hour; (d) severe toxic reactions to chlorpromazine. Tubocurarine, 15 to 20 mg., or gallamine, 40 to 60 mg., is given intravenously every one to three hours when jerk-like movements of the diaphragm and the lower jaw indicate the emergence of tetanus spasms.

Definitive relaxation therapy with either chlorpromazine or tubocurarine is continued unabated for 16 days, and then gradually withdrawn over a period of 7 to 10 days. During the withdrawal of tubocurarine, chlorpromazine, 0.3 mg. per kilogram per hour, is given intravenously, and this is in turn decreased gradually over four or five days. Thus the sedation-relaxation regime continues for at least 21 days in moderately severe cases and for 28 days in severe cases. Imperfect control and asphyxia are most likely during the introduction and withdrawal of this therapy. Haste may breed disaster if the patient is weaned off sedation and relaxation too quickly.

Tracheostomy and its Management.

A tracheostomy aims (a) to prevent asphyxia due to tetanic laryngeal spasm, (b) to permit efficient toilet of the bronchial tree, and (c) to permit the insertion of a cuffed rubber tracheostomy tube. It is required in all except the mildest cases of tetanus, and the slightest evidence of a spasm is an urgent indication.

Method.

General anaesthesia with endotracheal intubation is essential. A small transverse skin incision is made over the trachea at the level of the second tracheal ring. In certain people with short necks and/or large thyroid glands, it may prove necessary to divide the thyroid isthmus to display the trachea easily. The stoma is made with a transverse incision the full width of the trachea between the second and third rings, and the margins of this opening are sutured directly to the edges of the skin incision.

The site and size of the tracheostomy are vital considerations if maximum benefit and safety are to be ensured. Low in the neck just above the suprasternal notch the trachea is deeply placed, so that difficulty is encountered in suturing the skin to the trachea without undue tension and without narrowing the stoma; cuffed rubber tubes do not lie well here, and there is great risk of airway obstruction due to the carina itself or to endobronchial intubation. An opening above the first tracheal ring may lead to stenosis

¹As local manufacture has ceased, a special import licence is necessary for diallylbarbituric acid ("Dial", Ciba, 200 mg. per 2 ml. ampoule).

and damage of the larynx. The size of the tracheostomy should be sufficient to house Radcliffe (Spalding and Crampton-Smith, 1956) or James tubes as follows: No. 10 in adult males, No. 8 in adult females and adolescents, No. 4 and No. 6 in children. The appropriate tube is inserted in the operating theatre and the cuff is inflated. Haemostasis should be as perfect as possible, for blood in the bronchial tree causes collapse of the lung and reflexly exaggerates the tetanus.

Management.

Once the nose and throat are bypassed in this way, the bronchial mucosa becomes dry and infected and frequently desquamates. If a virulent staphylococcus gains foothold, a mortal infection results. Any mucosal lacerations due to careless or unnecessarily frequent aspirations of the trachea or to contamination with saliva increase the risk of infection. The following precautions are taken to avoid this. (i) With the tube *in situ* and the cuff inflated, the skin incision and hilt of the tube are swabbed every two hours with 1:1000 chlorhexidine solution, then dried; this prevents stagnation of secretions around the wound. (ii) The nose and pharynx are aspirated every two hours with a metal sucker. For nasal aspiration the sucker is inserted gently into the nostril, which is occluded over the sucker head till an airtight fit is obtained. Thus air is drawn through the nose from the pharynx, carrying saliva and mucus with it. The passage of rubber catheters into the nose for aspiration inevitably causes trauma to the vascular mucosa. (iii) Before aspiration of the trachea or removal of the tracheostomy tube, the hands are scrubbed, the neck area is swabbed with 1:100 chlorhexidine solution and the chest is draped. (iv) Blind aspiration of the bronchial tree via the tube is not done as a routine at any fixed period, but only as signs of accumulating secretions develop; in the absence of infection this implies every 8 to 12 hours, and with infection every two to four hours. (v) The cuff is never deflated and the tube is never changed unless the nose and pharynx are cleared completely just beforehand. (vi) The tracheostomy tube is changed once every 24 hours, and a sterile tube is reinserted; great care is taken not to tear the incision during insertion. (vii) Rubber catheters for tracheal aspiration have smooth tips. Suction is applied as they are slowly withdrawn; as the lumen opens on the side of the catheter, gentle rotation is essential for efficient removal of secretions; it is not necessary to push them vigorously back and forth in the bronchial tree. (viii) Under no circumstances is the equipment for aspiration of one patient used for another.

Bronchoscopy.

Bronchoscopy via the tracheostomy is performed every 24 or 48 hours, to inspect the bronchial tree and to ensure under direct vision the effectiveness of the aspiration.

Cough Therapy.

Repeated attempts to remove secretions from the segmental bronchi by blind aspiration through the tracheal tube are avoided by measures designed to dislodge mucus plugs and to deliver them into the trachea or into the endotracheal tube itself. Such measures attempt to reproduce the effects of a cough by a slow maximal chest expansion followed by a rapid deflation phase. The conventional respirator is set to do this as nearly as possible, and a vigorous, vibrating, manual compression of the chest is applied during the deflation phase to increase its rapidity. A cough exsufflator (Barach and Bickerman, 1956), set at +30 cm. of water and -30 cm. of water, is connected directly to the tracheal tube via a rigid, large-bore tube. This is capable of producing far more rapid deflation phases than the use of the conventional respirator. Five or six cycles are used, ending always with an inflation phase to expand the lungs fully. One or other method is employed every four to six hours, and always before tracheal suction.

Humidification.

Compressed air or oxygen from cylinders is completely dry and room air partly dry if compared with the full saturation of normal tracheal air; to retain effective ciliary action and to protect the mucosa from desiccation and from secondary infection, humidification and sometimes warming of the inspired gases are employed. A nebulizer with normal saline or a Spalding (Marshall and Spalding, 1953) humidifier is included on the inspiratory side of the respirator.

Use of Suction.

The degree of suction and the size of suction catheters are important considerations (Rosen and Hillard, 1960). Excessive suction aspirates pieces of the bronchial mucosa, producing hemorrhage and ulceration. A safe pressure range is 5.0 to 7.5 inches of mercury, and under no circumstances is 10 inches of mercury exceeded. During the actual aspiration of the bronchial tree, air is drawn into the catheter from the trachea, the bronchi and the lungs. If the diameter of the catheter is large compared with that of the tracheal tube, particularly if it blocks the tube completely, gross collapse of the lung may result. The following catheters are employed to lessen this danger: English gauge 3 for tubes size 4 to 6; English gauge 5 for tubes size 7 to 9; English gauge 6 for tubes size 10. Great care is taken to use suction intermittently and to restrict its duration to less than 45 seconds. This applies to patients with weak spontaneous respirations as well as to the apnoeic, for in the former all tidal exchange disappears quickly up the catheter. Exactly similar conditions exist during bronchoscopy—to ensure adequate oxygenation of the blood, brief periods of aspiration are alternated with periods of artificial respiration with 100% of oxygen.

Tracheal Necrosis.

The principal danger of the cuffed tube is pressure necrosis of the tracheal wall. Certain precautions are taken to avoid this risk. First, the cuff is deflated for a period of five minutes every two hours after complete nasopharyngeal toilet. During this time it may be necessary to cycle the respirator manually. Second, the cuff is inflated till it is just airtight at the peak of inspiration, and no more. The volume of air needed depends on the diameter of the tube in relation to that of the trachea and to the newness of the cuff itself. It rarely exceeds 4 ml. Tubes worn by repeated steam sterilization or by prolonged soaking in antiseptic solutions develop fragile, baggy cuffs. If these are inflated excessively, a bleb of the cuff may descend over the mouth of the tube, causing complete or partial respiratory obstruction. Cuffed rubber tubes are discarded as soon as loss of elasticity appears. A new type of tube has been designed with less irritating properties than the usual red rubber ones (Salt, Parkhouse and Simpson, 1960). These are to be tried in the near future.

As the tetanic process subsides, it is essential to ensure efficient power of swallowing and competence of the larynx before removing the tracheostomy tube permanently. Reeducation of the voice by periodically removing the tube and occluding the stoma is employed to restore laryngeal function. After the tube is removed, the tracheostomy closes spontaneously. Excision of the scar may be necessary some months later.

Artificial Respiration.

Although the tracheal stoma avoids asphyxia due to tetanic laryngeal spasms, asphyxia due to respiratory insufficiency may result from (a) poor control of muscle rigidity and generalized spasms, (b) profound muscle relaxation or central depression produced by the therapeutic agents. Although the ability to produce muscular relaxation without depression of lung ventilation has been sought for many years, this ideal balance is not possible in dealing with the constantly labile tetanic process. In practice, patients with tetanus are considered to be on the verge of respiratory failure throughout the course of disease. For this reason some form of artificial respiration is required for all except the mildest cases.

Type of Artificial Respiration.

The tank respirator (the original "iron lung") is not used in this hospital, because it is not possible to nurse the enclosed patient adequately without repeatedly suspending the artificial respiration. Instead intermittent positive pressure (I.P.P.) or positive-negative pressure (P.N.P.) is applied directly to the patient's airway via the tracheostomy tube. (In this context, a pressure is regarded as positive or negative when referred to the atmospheric pressure.) Such positive pressure can either

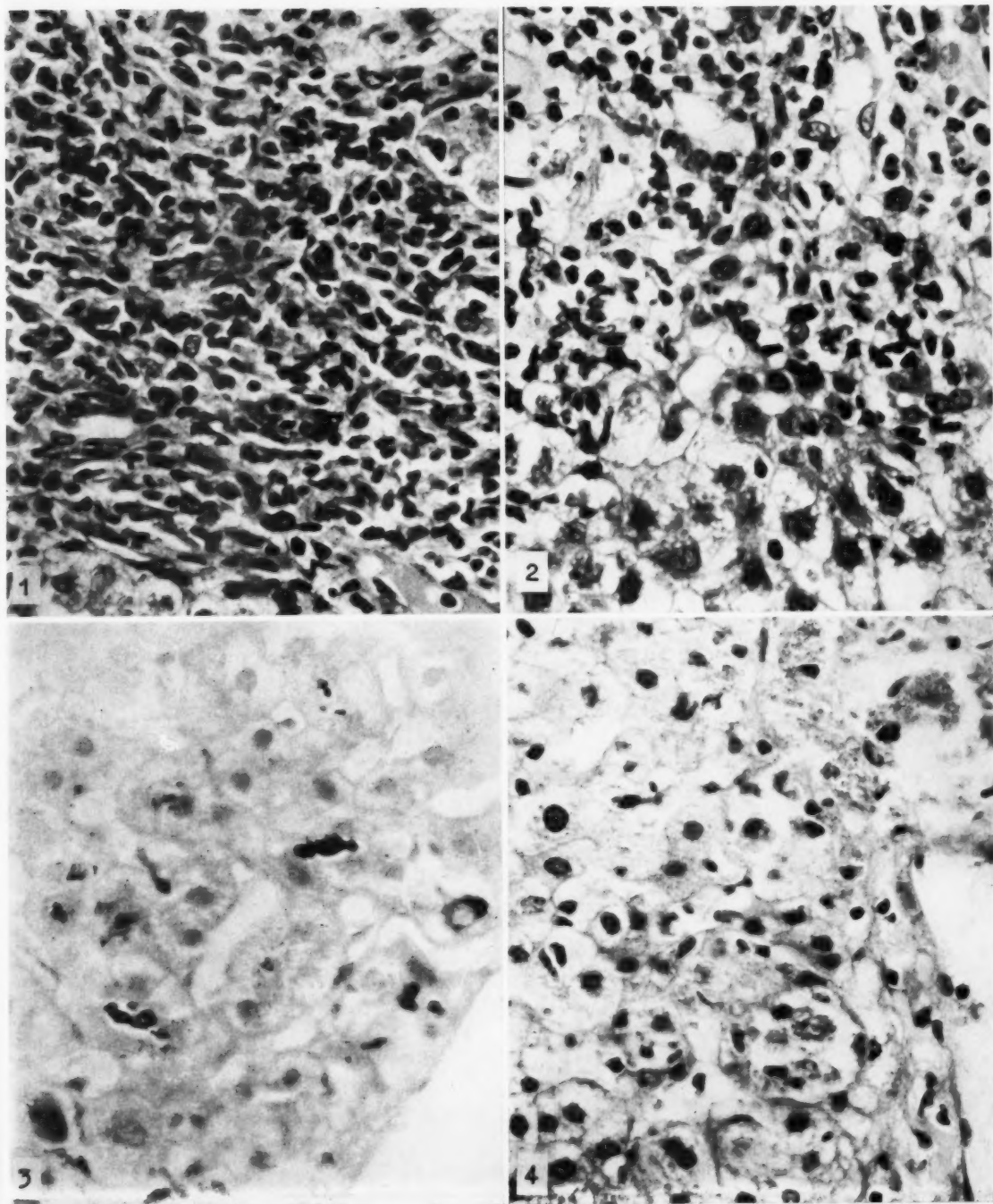
ers
(50).
osa,
ure
um-
tne
into
ngs.
that
ube
The
ger:
for
reat
rict
to
s to
ears
xist
a of
with

sure
are
or a
aso-
sary
ated
l no
eter
the
ubes
nged
uffs.
may
e or
are
type
rties
and
ture.
asure
rynx
ntly.
tube
ngeal
tomy
eces-

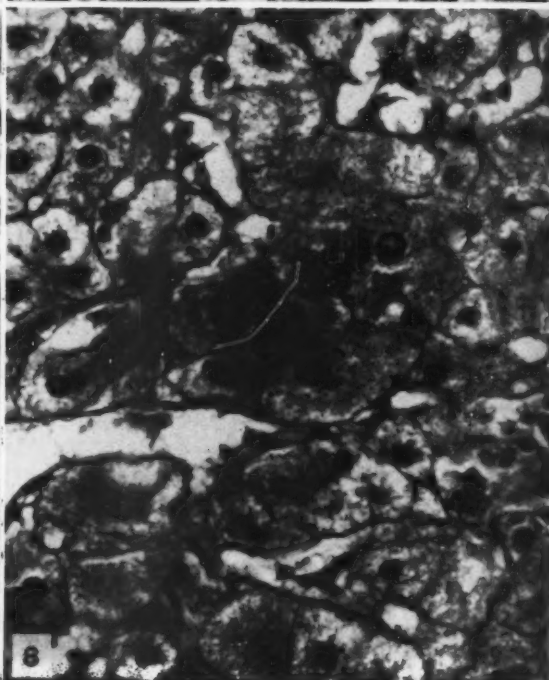
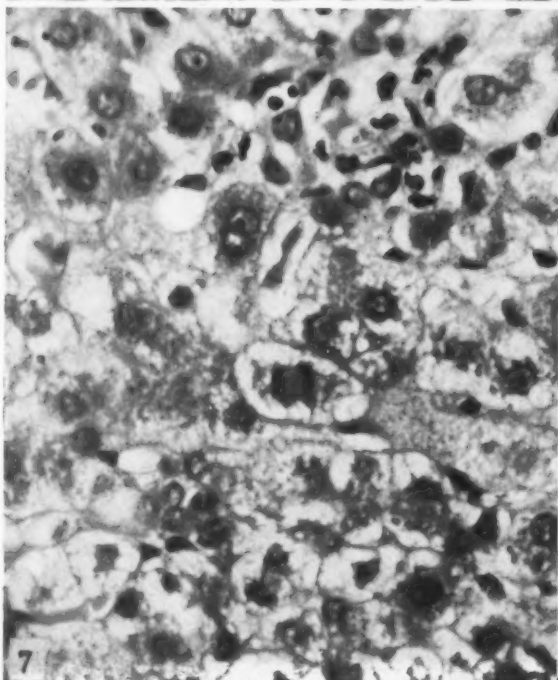
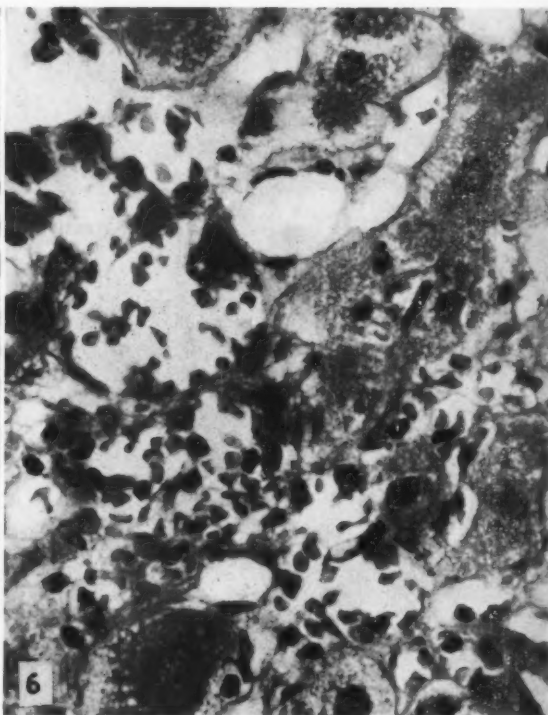
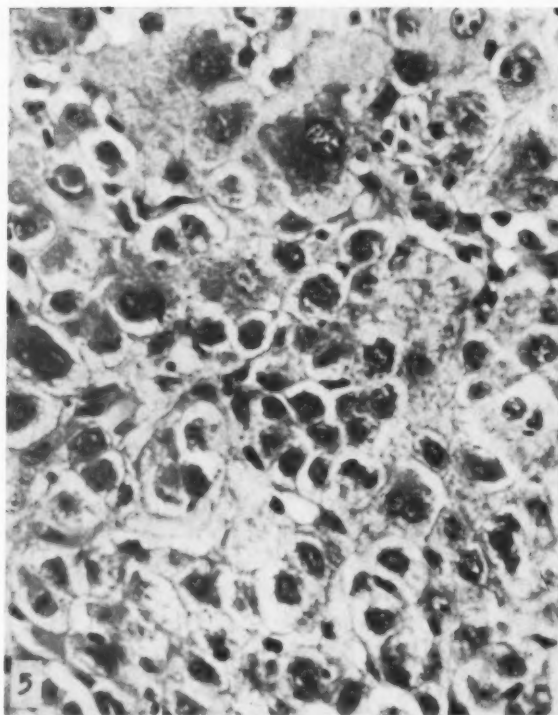
to
atory
uscle
uscle
hera-
cular
has
not
tanic
dered
t the
ifical
cases.

s not
nurse
sus-
ittent
essure
y via
ure is
o the
either

ILLUSTRATIONS TO THE ARTICLE BY R. A. JOSKE, L. R. FINLAY-JONES AND E. G. SAINT.



ILLUSTRATIONS TO THE ARTICLE BY R. A. JOSKE, L. R. FINLAY-JONES AND E. G. SAINT.



assis
mach
and
gene
mach
patie
is g

As
respi
respo
the
of th
in so
the
high
press
hyper
the
to p
ensu
for
been
of no
const
giver
poor
of th
disad
atten
tion
gene
thorax
(b)
accid
tion

Con
respi
venot
so th
to p
(Gor
respi
essen
minu
(c)
preve
depre
"figh

Ch
emple
the a
With
ideal
régim
partia
usual
the
deper
avala
emple
Clark

In
expan
to m
as th
logy
Duboi
is do
press
the n

* Bi
218 F
* Be
Angel
* Sm
Engla

assist or control respiration. In assisted ventilation the machine is set to augment spontaneous weak respirations, and the energy to initiate the inspiratory phase is generated by the patient. In controlled ventilation the machine provides the total respiration in the apnoeic patient, and the energy to initiate the inspiratory phase is generated by the machine itself.

Assisted Respiration.—To be capable of assistance, a respirator has a "trigger" mechanism, which is fired in response to the negative airway pressures generated by the patient's spontaneous inspirations. The sensitivity of the trigger varies from one machine to another, and in some it can be varied by a special control. It has the following disadvantages: (a) If the sensitivity is high, cycling begins as a result of the slightest negative pressure in the air passages. Tachypnoea with gross hyperventilation ensues. (b) If the sensitivity is low, the spontaneous inspiratory efforts may be too weak to produce cycling at all. Apnoea with eventual asphyxia ensues, unless an automatic cut-in device is available for controlled ventilation, and unless this device has been preset. (c) In the therapy of tetanus the amount of negative pressure generated by the patient fluctuates constantly. It is low when large doses of relaxants are given, but also when thoracic rigidity is great owing to poor control of the tetanic process. Thus the sensitivity of the trigger requires variation from hour to hour. These disadvantages do not become dangers unless the medical attendant is uninformed or inattentive. Assisted respiration has the following advantages: (a) As the patient generates some negative intrapleural pressure, the thoracic pump aiding venous return is not lost completely. (b) If the machine is disconnected from the patient accidentally or intentionally, sufficient spontaneous respiration may remain to delay asphyxia by five to 10 minutes.

Controlled Respiration.—The disadvantages of controlled respiration are as follows: (a) During control, aid to venous return by the thoracic pump is lost completely, so that great care must be taken in setting the respirator to provide the ideal "waveform or pressure curve" (Gordon, Frye and Langston, 1956). (b) To control respiration effectively, complete relaxation and apnoea are essential. In this state, asphyxia occurs in two or three minutes if the patient is disconnected from the machine. (c) In some cases of tetanus, the relief of rigidity and prevention of spasms are attained with but the slightest depression of spontaneous respiration. Such a patient "fights" a respirator set to control ventilation.

Choice of Method.—The type of artificial respiration employed in a case of tetanus depends principally upon the amount of relaxation needed for adequate therapy. With the chlorpromazine-barbiturate régime, assistance is ideal and control virtually impossible. With the curare régime, although assistance is theoretically possible by partial curarization, in practice control of ventilation usually supervenes, for spontaneous breathing ceases in the wake of mechanical over-ventilation. The choice depends to a certain extent on the type of respirator available—a patient-triggering device is required to employ assisted breathing. Bird¹, Bennett², and Smith-Clarke³ respirators are used at this hospital.

Mechanics of Respirators.

In breathing a certain amount of energy is needed to expand the lungs and chest, to set air into motion and to move it into the alveoli. This energy is referred to as the work of breathing, and this part of lung physiology as the mechanics of respiration (Comroe, Forster, Dubois, Briscoe and Carlsen, 1955). Normally the work is done by the respiratory muscles, but with positive pressure ventilation it is done entirely or partially by the respirator. The pressure generated in the airway

and/or by the machine is a measure of the work performed.

Two components are considered in the work of breathing, compliance and airway resistance.

Compliance.—The elastic and viscous properties of the lung and chest wall are referred to in terms of compliance. The greater the compliance, the less the work required to overcome these elastic and viscous properties, and vice versa. Compliance is decreased with rigidity of the chest wall as in tetanus and in the older age groups, with obesity, and with infection, edema, congestion and fibrosis of the lung. In such states the greater work required to produce satisfactory tidal exchange is reflected by increased respirator settings and greater positive airway pressures. This component is measured by the change in lung volume produced by a unit change in airway pressure—that is, litres per centimetre of water pressure—a measurement of static conditions.

Airway Resistance.—A certain amount of work is expended in setting air into motion and in overcoming the frictional resistance offered by the bronchial tree

TABLE II.

Component.	Normal, Relaxed Patient.	Relaxed, Intubated Patient.
Total compliance ..	0.1 litre per centimetre of water.	0.05 litre per centimetre of water.
Airway resistance ..	2 centimetres of water per litre per second.	4 to 6 centimetres of water per litre per second (up to 12).

to air movement. This component is increased by oedema of the bronchial mucosa, by bronchospasm and by accumulated secretions, and, because frictional resistance increases with increased rates of movement, it is increased during rapid breathing. An endotracheal tube of large bore (size 10) offers more resistance than the normal respiratory passages. An idea of the mechanics of ventilation can be obtained from Table II.

To give a tidal volume of 500 ml. in one second, the following components are required:

Normal, relaxed subject:	
Compliance	5 cm. of water
Resistance	1 cm. of water
Total	6 cm. of water
Relaxed, intubated subject:	
Compliance	10 cm. of water
Resistance	2 cm. of water
Total	12 cm. of water

The same work may be required for children as for adults, because, although compliance tends to be greater in the child, airway resistance is greater, owing to the narrow air passages and the rapidity of breathing.

The pressures referred to so far are those measured in the mouth or the endotracheal tube. Artificial respirators record the pressures some three or four feet from the patient, and a certain amount of work is expended in the connecting tubes, which have compliance and resistance factors of their own. When all these factors are considered, a pressure of 15 cm. of water generated and/or measured by the respirator is ideal in all patients with normal lungs. In tetanus, a pressure of 20 cm. of water is ideal, but if obesity or lung disease is present as well, a pressure of 25 to 30 cm. of water may be required to provide adequate tidal exchange.

General Practical Aspects of Respirators.

Leaks.—An essential requirement for efficient I.P.P. and P.N.P. is an airtight connexion from the machine to the patient's trachea. This is ensured by the adequately inflated cuff of the tracheostomy tube. Although leaks occur most commonly at the trachea, they may develop anywhere in the system, from the source of pressure in the machine to the patient.

¹Bird, Mark VIII, Bird Oxygen Breathing Equipment Inc., 218 Fremont, San Francisco 5, California.

²Bennett I.P.P., V. Ray Bennett and Associates, Los Angeles 48, California.

³Smith-Clarke, The Cape Engineering Co. Ltd., Warwick, England.

The Expiratory Phase.—The use of a closed system with soda lime for carbon dioxide absorption proves unwieldy and expensive for long-term artificial ventilation. Instead, a semi-closed system is employed by placing a one-way valve close to the patient. This prevents excessive dead space and permits expiration into the atmosphere.

High Concentrations of Oxygen.—Ventilation with high concentrations of oxygen is unnecessary and, in fact, undesirable. First, if lung ventilation is adequate and pulmonary collapse absent, high oxygen tensions do not increase the blood oxygen content significantly. Second, during hypoventilation with 100% oxygen, hypercarbia is possible without signs of hypoxia. Third, if a plug of mucus blocks a bronchus, distal collapse will occur rapidly if 100% oxygen is present, but slowly if 79% of nitrogen is present. The nitrogen of the air, being inert, acts as a scaffold, delaying complete collapse for 12 to 16 hours. However, used in emergencies and just before tracheal aspiration, ventilation with 100% oxygen may be life-saving.

Volume or Pressure Cycling.—There are hundreds of respirators available. They have been classified elaborately from a mechanical point of view, but, in practice, the only distinction of importance concerns the difference between volume and pressure cycling at the end of the inspiratory phase. A machine is volume cycled when the inspiratory phase terminates after a preset volume has been ejected. If a leak develops in the system, the machine continues to eject the preset volume, and a part of this, equal to the leak, is lost to the atmosphere. If airway obstruction occurs, such a machine continues to eject the preset volume, so that there tends to be over-expansion of unobstructed lung areas or relief of obstruction. In ejecting this same volume under these circumstances, a greater airway pressure will be reached and recorded by the respirator. A machine is pressure cycled when the inspiratory phase terminates at a certain preset pressure. If lung compliance is low, tidal volume may be dangerously low at conventional pressure settings. If a leak occurs in this system, such a machine develops a very long inspiratory phase or ceases to cycle, because the preset pressure cannot be reached. If airway obstruction occurs, the machine will cycle rapidly and produce poor tidal exchange.

Setting the Respirator.

Nomograms are available to estimate the ideal tidal volume for the particular age, sex and surface area of the patient. Corrections are included for pyrexia, high altitudes, tracheostomy and respiratory acidosis.

If the respirator is volume cycled (Smith-Clarke), it is set to deliver the ideal tidal volume 12 to 15 times a minute, and as a result it will record an airway pressure between 15 and 20 cm. of water. If the respirator is pressure cycled (Bird, Bennett), it is set at a pressure of 20 cm. of water and a rate of 12 to 15 cycles a minute. After the initial setting a constant check is made to ensure adequacy of pulmonary ventilation. As pulmonary complications arise, it will be necessary to increase the original setting. The following points are important in the setting of ventilation: (a) careful inspection to ensure that chest expansion looks normal; (b) measurement of chest expansion at two levels with a tape measure; (c) a Wright ventilation meter (Muschin, and Rendell-Baker, 1959) placed in the system close to the patient to measure the actual tidal exchange; (d) daily estimates of the serum bicarbonate content (low levels indicate respiratory alkalosis, high levels, acidosis); (e) estimation of the oxygen saturation and partial pressure of carbon dioxide in samples of arterial blood; if facilities are available, such estimations should be made daily.

At the commencement of respirator therapy, a sample of arterial blood is taken to test whether the estimated ideal setting is adequate to ventilate the lungs. If necessary, the setting is altered until normal arterial gas contents are produced. When the actual ideal setting is

found, measurements of chest expansion and tidal exchange are made, and from then on these can be used as additional readily available checks of ventilation.

Estimates of the carbon dioxide content of end-tidal samples of expired air are useful in assessing ventilation, but so far in the therapy of tetanus they have not been employed in this hospital.

Danger of Positive Pressure Ventilation.

Over-Ventilation.—Rupture of lung tissue leading to pneumomediastinum and pneumothorax need not be considered as risks with intrapulmonary pressures less than 40 cm. of water, even with the uneven distribution that may occur in an emphysematous lung. All respirators have a safety blow-off valve set between 30 and 40 cm. of water.

The application of positive airway pressure decreases the intrapleural negative pressure pump. Thus venous return is hampered and systemic arterial flow will tend to fall. Under ideal physiological conditions, a compensatory rise of peripheral venous tone restores a satisfactory venous gradient to fill the atria adequately. In severe disease, and particularly in states of oligemia, such compensatory mechanisms are lacking and marked hypotension results. The positive pressure is applied to the pulmonary capillaries, where the mean pressure is about 10 cm. of water. This strains particularly the right ventricle. To minimize the deleterious effects on the circulation, the mean airway pressure during each respiratory cycle is kept as low as possible by (a) a short inspiratory phase not greater than one second in duration, (b) an expiratory phase at least twice as long as the inspiration, (c) a negative airway pressure of 5 to 7 cm. of water during expiration. (Excessive negative pressures tend to collapse small bronchioles.)

Excessive respiratory alkalosis has undesirable consequences. There is generalized, but more importantly cerebral and coronary, vasoconstriction (Kety and Schmidt, 1946). A Bohr effect is seen on the oxygen dissociation curve of hemoglobin, so that oxygen is released less readily to the tissues. Both these effects prejudice the oxygen supply to the tissues. The rise of pH causes a fall in the ionized calcium fraction of the plasma, leading eventually to tetany with its effects upon the conducting and contracting cardiac tissues. Systemic hypotension and arrhythmias due to relative hypokalaemia appear.

Hypoventilation.—Hypoxia is the most disastrous sequel of hypoventilation. It can produce anything from a mild sympathomimetic response to complete cardiovascular collapse. The sensitivity of vital neural tissues to hypoxia is well known.

In asphyxia, signs of hypoxia accompany and usually overshadow those of hypercarbia. Signs of hypercarbia can occur alone during hypoventilation with high concentrations of oxygen. They consist of salivation, bronchorrhoea, sweating and flushing, pyrexia, extrasystoles, rise of systolic and pulse pressures and, with arterial carbon dioxide tensions of 100 to 120 mm. of mercury, coma and papilloedema. Heavy sedation masks to a great extent all the signs of hypercarbia (McCardle, Roddie, 1958). The sudden relief of hypercarbia by over-ventilation may lead to ventricular arrhythmias due to changes in the distribution of potassium within the body.

Hypoventilation also leads to inadequate expansion of segments of the lung, with retention of secretions and eventual collapse of lung tissue.

Eradication of the Disease.

As was mentioned under preliminary therapy, a subcutaneous test dose of tetanus antiserum is given (Laurent and Parish, 1952). If a systemic histamine release reaction has not appeared after 45 minutes, 100,000 units of tetanus antiserum are infused in 250 ml. of normal saline. If a systemic reaction appears, desensitization is carried out. No further attempts are

made during the course of the disease to increase the blood level of antiserum.

The wound of entry is treated on general surgical lines. Infected discharging puncture sites are excised as completely as possible, surrounding functional tissues being conserved. Dirty abrasions are subjected to thorough *débridement*. Foreign bodies are removed, provided that they are not so multiple or so widely scattered, so deeply placed or so closely related to vital structures, as to render removal a major operation. If practicable, 10,000 units of tetanus antiserum are infiltrated locally. Procaine penicillin, in a dosage of 1,000,000 units every eight hours, is given for seven days.

Active immunization with tetanus toxoid is started eight weeks after the therapeutic dose of antiserum. It is intended to adopt as a routine the use of an immunization card similar to the one mentioned by Ackland (1959).

Intravenous Therapy.

During the three to five weeks' period of sedation, relaxation and artificial respiration, accurate water and electrolyte balances are maintained, and caloric intake is kept sufficient to spare protein breakdown as much as possible. Intragastric and intravenous routes are available, and each has disadvantages.

Intragastric feeding predisposes the patient to regurgitation and vomiting, particularly as gastric dilatation and paralytic ileus are not uncommon complications in these acutely ill patients. Gravitation into the lung is very likely because of the therapeutic depression of laryngeal reflexes. The cuffed tube affords the sole protection against this. Absorption of chlorpromazine by the gastro-intestinal tract is uncertain, and that of the neuro-muscular blocking agents negligible.

The risks of prolonged intravenous therapy are thrombosis and septicæmia; but, as the therapy of tetanus demands continuous prolonged administration of drugs, it offers simplicity, accuracy and rapidity of action. The last-mentioned is important, owing to the rapidly fluctuating course of the disease. Thus the use of the intravenous route becomes almost a necessity, and it is not difficult at the same time to infuse the daily requirements of water, calories and electrolytes. Chlorpromazine and hypertonic solutions induce rapid thrombosis of peripheral subcutaneous veins, so that to ensure infusions for three to five weeks a plastic cannula is inserted into an innominate or common iliac vein.

Special giving sets are made with three "Tuta" plastic disposable sets and two Y-piece connectors, to permit the administration of three infusions through the one plastic cannula. Each set is sealed in a paper bag for sterilization in ethylene oxide,^a a toxic gas that does not damage plastics. A special autoclave is necessary to employ this agent.

The venous cannulation is done with full aseptic precautions in the operating theatre under general anaesthesia. A small skin incision is made just above the elbow or in the groin and, under direct vision, a sufficient length of gauge 3 "Polythene" is inserted to reach the innominate or common iliac vein respectively. It is connected by a gauge 16 French venesection needle to the piece of rubber tubing of the giving set. Checks are made for leaks and for cessation of flow on altering limb posture. Common sites of leakage are the needle-"Polythene" junction and the vein itself. Blockage due to posture is seen exclusively in the arm with flexion of the elbow and/or abduction of the shoulder. Gradual withdrawal or further insertion will find the site appropriate for maximum efficiency of flow. After suture, the wound, the "Polythene" tubing and the needle connector are enclosed in a sealed dressing with "Mastisol" and "Elastoplast".

^a Supplied by Tuta Products, 10 Vere Street, Collingwood, Melbourne.

^b Gaseous Sterilizing Agent, American Sterilizer, Erie, Pennsylvania.

The following precautions are taken to lessen the risk of septicæmia. (a) Injections are never given into the transfusion set except in a dire emergency. (b) Hands are washed thoroughly before bottles are changed or loaded with drugs. (c) Every effort is made to avoid blockage due to posture of the limb, accidental over-clamping of the tube, or a bottle being allowed to run through. (d) If blockage has occurred and is recent, an attempt is made to syringe through with full aseptic precautions. (e) The site of infusion is changed every seven days, arm to groin to arm to groin.

In practice, the special set is employed as follows. One part is concerned with the administration of most of the daily requirements of water, calories and electrolyte, so it is referred to as the "main drip". The second part is concerned with the intermittent administration of chlorpromazine or tubocurarine, each of which is loaded into the bottle at the start of each day. The third part permits the slow infusion of potassium solutions, antibiotics, and protein hydrolysates. All urine and any aspirated gastric contents or saliva are saved, and their daily volume and electrolyte content are measured. The collection of urine in males is by Penrose tubing with or without suprapubic pressure or by intermittent catheterization, and in females by an indwelling self-retaining catheter. Insensible loss of water by the skin is estimated as 600 ml. per square metre of surface area per day, and that of salt as 4 mEq per square metre of surface area per day (Merrill, 1955). The latter increases to 8 mEq per square metre per day with the onset of sweating. Thus accurate replacement is possible without reference to the serum electrolytes. However, these are estimated each day as additional checks. Concentrated glucose solution and 10% alcohol (Merrill, 1955) supply at least 1400 calories daily. Vitamin C (100 mg.) "Combex" (2 ml.) and vitamin K analogue (10 mg.) are given intramuscularly every third day.

Prevention of Infection.

Infections of the lungs, the blood-stream and the bladder are continual hazards during the prolonged period of intensive care. The dangerous offending organisms are *Staphylococcus pyogenes*, *Pseudomonas pyocyanea* and *Bacterium coli*, originating from doctors, nurses, other patients, ward dust and inadequately sterilized respirator equipment. General measures to lessen these risks of infection are as follows. (a) Patients are nursed in a special ward or room. (b) All attendants have nasal swabs examined, and no person harbouring a resistant staphylococcus is permitted in the ward. (c) Visitors to the ward, including doctors, nurses, students, technicians and physiotherapists, are reduced to an absolute minimum. (d) Any person in the ward is masked continually. (e) Cleaning routines are similar to those employed in an operating theatre, special attention being given to beds and to oxygen cylinders, and their carriers. (f) Attendants scrub up before handling the tracheostomy area or the transfusion bottles. (g) Chlorhexidine and "Lysol" are the only antiseptics used. (h) Plastic or rubber non-disposable equipment is sterilized in ethylene dioxide.

Pneumonia is secondary to bronchitis, and certain preventive measures have been mentioned in the discussion of the tracheostomy. Tracheal swabs taken every third day are sent for culture and antibiotic sensitivity tests. When bronchitis inevitably supervenes after seven to 10 days with the production of mucopurulent secretion, appropriate antibiotic therapy can be started immediately. Systemic administration is employed as a routine, but antibiotic aerosols for intrabronchial use are on trial at the present time.

At the weekly change of the "Polythene" catheter, a wound swab and the used catheter itself are sent for culture. If a growth occurs from these, blood cultures are taken and antibiotic therapy is commenced with broad-spectrum drugs. "Chloromycetin" with erythromycin or vancomycin is the most valued combination, in

view of the sensitivity of prevalent microorganisms in the hospital. However, streptomycin is of particular value with certain strains of *Pseudomonas*.

Conclusion.

In conclusion, it should be emphasized that the success of management rests squarely on the shoulders of those constantly on duty in the ward. The tenacity and patience of the resident medical officers and nurses in their prolonged vigil are appreciated throughout the hospital.

Summary.

1. The importance of a special unit and team for the management of tetanus is stressed.
2. Tetanus is controlled by sedation with a barbiturate and by relaxation with chlorpromazine or tubocurarine.
3. Tracheostomy is almost a routine requirement. Its management is analysed.
4. Artificial respiration is discussed from the theoretical and practical aspects.
5. Intravenous therapy and prevention of infection are discussed.

References.

- ACKLAND, T. H. (1959), "Tetanus Prophylaxis", *MED. J. AUST.*, 1: 185.
- BARACH, A. L., and BICKERMAN, H. A. (1956), "Pulmonary Embphysema", Williams & Wilkins, Baltimore: 194.
- COMROB, J. H., FORSTER, R. E., DUBOIS, A. E., BRISCOE, W. A., and CARLSEN, E. (1955), "The Lung", Year Book Publishers: 113.
- GOODMAN, L. S., and GILMAN, A. (1955), "Pharmacological Basis of Therapeutics", Macmillan, New York: 137.
- GORDON, A., FRYE, W., and LANGSTON, H. (1956), "Cardio-respiratory Dynamics of Controlled Ventilation in the Open and Closed Chest", *J. thorac. Surg.*, 32: 413.
- LAURENT, L. J. M., and PARISH, H. J. (1952), "Serum Reactions and Serum Sensitivity Tests", *Brit. med. J.*, 1: 1294.
- MARSHALL, J., and SPALDING, J. M. R. (1953), "Humidification in Positive Pressure Respiration for Bulbospinal Paralysis", *Lancet*, 2: 1022.
- MERRILL, J. P. (1955), "The Treatment of Renal Failure", Grune & Stratton, New York: 83, 90, 91.
- MUSCHIN, N. W., and RENDELL-BAKER, L. (1959), "Automatic Ventilation of the Lungs", Blackwell, Oxford: 30 (Wright Ventilation Meter), 150 (Bird), 216 (Bennett), 242 (Smith-Clarke).
- SALT, R. B., PARKHOUSE, J., and SIMPSON, B. R. (1960), "Improved Material for Radcliffe Tracheostomy Tubes", *Lancet*, 2: 407.
- ROBSON, J. M., and KEELE, L. A. (1956), "Recent Advances in Pharmacology", Churchill, London: 153.
- ROSEN, M., and HILLARD, E. K. (1960), "The Use of Suction in Clinical Medicine", *Brit. J. Anaesth.*, 32: 486.
- SPALDING, J. M. K., and CRAMPTON-SMITH, A. (1956), "A New Tracheostomy Tube", *Lancet*, 2: 1247.

A MINIATURE PACE-MAKER FOR DIRECT STIMULATION OF THE MYOCARDIUM.

By DOUGLAS COHEN, M.S., F.R.A.C.S.; VICTOR HERCUS, M.B., M.R.C.P. (Ed.), D.A.; A. C. BOWRING, M.B., F.R.C.S., F.R.C.S. (Ed.); and E. C. HULME.¹

From the Adolph Basser Institute of Cardiology, Royal Alexandra Hospital for Children, Sydney.

THE use of direct stimulation of the myocardium in complete atrio-ventricular dissociation has been shown to be of considerable value in increasing the critically low ventricular rate that is present, and thus in improving the cardiac output until a normal rhythm is restored. Direct stimulation of the heart has been shown to be more efficient than external stimulation through the chest wall by skin electrodes. This latter technique is not well tolerated by the patient, since it may be associated with numerous undesirable side effects, which cause considerable distress to the patient. The use of a direct myocardial

electrode enables the stimulus to be applied with a relatively small voltage, and has been adopted for prolonged periods in the management of complete heart block after open heart surgery, and in selected cases of acquired complete heart block producing recurrent Stokes-Adams attacks.

It was thought that a suitable pace-maker should fulfil the following criteria before it was acceptable for clinical use: (i) The stimulus must be uniform and of relatively short duration. (ii) The stimulating voltage should be capable of variation from zero to 6 volts. (iii) The number of stimuli should be capable of being varied from 50 to 200 impulses per minute. (iv) The power source should be contained within the apparatus, capable of easy renewal and sufficient to last for at least one week without alteration in output. (v) The current delivered

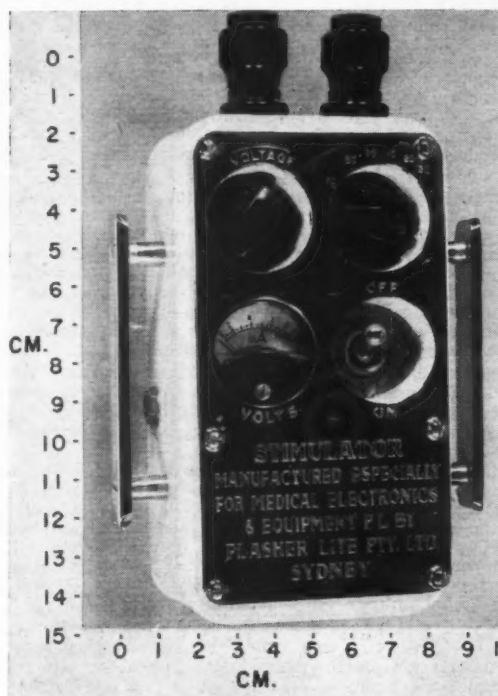


FIGURE 1.
The miniature pace-maker.

to the myocardium should be of such a nature as to produce a minimal amount of myocardial fibrosis about the stimulating electrode. (vi) Alterations in voltage or rate should not be capable of being affected accidentally. (vii) The entire apparatus should be light enough to be carried about by the patient without inconvenience. (viii) All leads should be capable of sterilization by standard techniques, and the wire should be sufficiently rugged in construction to minimize any risk of fracture after its implantation in the myocardium. The wire should not cause a significant amount of resistance to the current passing and should not be so thick as to cause any difficulty in insertion or subsequent removal.

When the electronic circuits were determined it was possible to construct a unit, illustrated in Figure 1, which fulfilled all the criteria set forth above. One of us (E.H.) had already constructed a lightweight transistorized unit capable of delivering a constant repetitive electrical stimulus, which had been devised to activate a light source. It was found that this could be adapted for our

¹Consulting Electronic Engineer to the Adolph Basser Institute of Cardiology.

purpose, with minor alterations designed to provide an output in the required range, and with the addition of two variable potentiometers for varying the stimulus rate from 50 to 200 impulses per minute and the output from zero to 6 volts.

The power source is provided by four standard dry cells contained within the unit.¹ Alternatively, an input jack is provided for connexion to a rather larger dry-cell battery for prolonged use.² Two stainless steel leads are used, consisting of multi-strand stainless steel wire and insulated by "Teflon" sheaths. One of these leads is embedded in the ventricular muscle and fixed to the epicardium by two or three fine silk sutures. The indifferent electrode of similar construction is fixed in the subcutaneous tissues of the chest wall. Only a very small voltage is required for impulse formation. The impulse is of less than 2 milliseconds' duration and rises rapidly in a sharply peaked wave form, falling almost as rapidly as it rises.

In practice, the rate is set to conform with the normal heart rate of the patient. A low-voltage setting is used initially, and this is gradually increased until a satisfactory ventricular rate is produced and maintained. Thereafter the voltage requirements are generally constant within the range 0.5 to 1 volt. Infection about the leads has not so far been a trouble, but this aspect would doubtless merit serious consideration should it be necessary to retain the leads for more than one or two weeks. In such instances the use of a miniature coil, totally embedded within the body of the patient and excited by a primary coil placed over it on the surface of the body, may be preferable, since this would eliminate all external connexions. Such an inductive type pace-maker is, at the moment, under construction.

The equipment described has had adequate laboratory testing and has proved satisfactory in clinical use. It is considerably less expensive than comparable overseas models, and is readily available from local sources.³

Description of the Unit.

The unit is 4.75 in. high by 2.5 in. wide by 1.75 in. deep, and weighs 15.5 oz. The back cover can be unscrewed for ready replacement of the four small batteries.

On the top of the unit are two output jacks, which are connected to the myocardial and indifferent electrodes. These are interchangeable, and they may be connected to a push-in type fitting or the wire may be screwed directly on to them if that is desired.

On the side of the machine is an input jack for connexion to a larger battery source, for use if it is intended to run the machine continuously for more than one week. This will save drain on the smaller batteries contained within the unit. When the unit is connected via this input jack to the larger battery, the smaller batteries within the unit are automatically disconnected; their power is thus conserved. This arrangement facilitates any battery-changing required whilst the machine is in operation, since the two alternative power sources ensure continuous functioning of the unit whilst either one is being changed.

The front panel is protected by an engraved stainless steel plate, and has two variable controls (for the rate and voltage output) which are recessed so that they cannot be altered accidentally.

Below these two controls are a voltmeter, indicating the output per impulse, and an on/off switch.

The entire unit is housed in a plastic case of solid construction, and two chromium metal bars are supplied on each side so that it may be conveniently strapped to the bed or carried by the patient, as desired.

¹ "Eveready" 1.5 volt batteries, No. 915AA.

² "Eveready" 6 volt battery, No. 509. (These will operate the unit with constant output for two to three months.)

³ Medical Electronics and Equipment Pty. Ltd., 1 Shirlow Street, Marrickville.

Summary.

A compact, pocket-sized, fully transistorized unit for myocardial stimulation by direct myocardial electrodes is described.

Reports of Cases.

CHLORPROMAZINE GIVEN ORALLY IN THE TREATMENT OF SEVERE TETANUS: A CASE REPORT.

By I. MADDOCKS¹

AND

J. K. DAWBORN²,

From the Clinical Research Unit of the Royal Melbourne Hospital and the Walter and Eliza Hall Institute of Medical Research, Melbourne.

THE treatment of severe tetanus by chlorpromazine given parenterally has been described by Packard *et alii* (1958), by Laurence *et alii* (1958), by Shanker and Mehrotra (1959) and by Benjamin (1960). We wish to present a severe case of tetanus in which chlorpromazine was required in large doses and was effective when given orally. It was supplemented by paraldehyde given by mouth.

Clinical Record.

A boy, aged 12 years, trod on a bone, causing a minor penetrating wound to the foot. At no time had he received anti-tetanic serum or tetanus toxoid. Seven days later he developed a stiff neck, with progression in eight hours to severe tetanus.

He was then admitted to the Royal Melbourne Hospital under the care of Dr. Ian Wood, to whom we are grateful for permission to publish this case. Full doses of anti-tetanic serum and penicillin were given, tracheotomy was performed and oral feeding by the intragastric drip method was initiated. Treatment was continued with chlorpromazine by intravenous infusion in a dose of 300 mg. per day. This was augmented during severe spasms by intravenous injections of 25 to 50 mg. of the drug. "Sodium Amytal", 200 to 300 mg., was also required; however, this caused respiratory depression and pronounced drowsiness and was therefore replaced by paraldehyde given orally, which proved to be much more effective.

Spasms increased in number and severity over the first three days. Chlorpromazine failed to control spasms until a level of 1500 mg. (36 mg. per kilogram) per day was reached and paraldehyde was added, oral doses of 32 ml. being given daily (Figure 1). However, intravenous infusion was discontinued on the sixth day, because this was causing extensive local thrombophlebitis and oedema of the limbs. Chlorpromazine and paraldehyde were therefore both given by the intragastric drip method, the doses remaining the same. During the ensuing three weeks the doses of chlorpromazine and paraldehyde were raised or lowered according to the frequency of spasms. It was found advantageous to reduce tracheotomy toilets to a minimum.

Definite improvement began from the nineteenth day, allowing the doses of chlorpromazine and paraldehyde to be reduced. Spasms ceased on the thirtieth day, and the tracheotomy tube was removed on the thirty-fifth day, when the dose of chlorpromazine was 100 mg. per day. The liver function tests and blood picture had remained normal throughout.

As sedation was decreased, a hyperexcitable mental state occurred which was associated with an abnormal

¹ Formerly Drug Houses of Australia Research Fellow.

² Drug Houses of Australia Research Fellow.

thirst, the daily fluid intake and output being up to eight litres. Both conditions gradually subsided, and on his discharge from hospital six weeks after admission, the patient was well, apart from some contraction of the calf muscles.

Discussion.

The incubation period of seven days and the rapid march of symptoms over eight hours show that this case was severe. The initial daily intravenous dose of 300 mg. of chlorpromazine was inadequate. The severity of spasms increased until the dose was raised to 1500 mg. per day. This proved highly effective.

Major spasms decreased on the sixth day, when maximum doses of chlorpromazine and paraldehyde were given. Minor spasms were frequent until the twelfth day. Occasional spasms, muscle rigidity and opisthotonus persisted for three weeks. As the doses of chlorpromazine and paraldehyde were altered con-

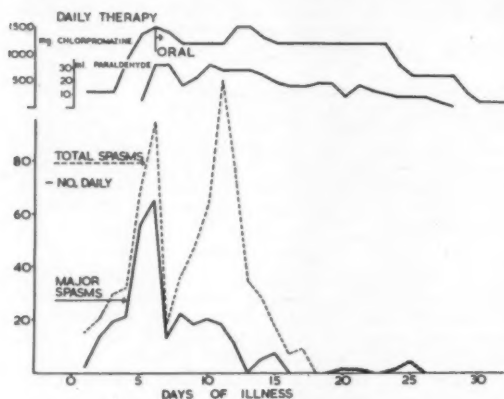


FIGURE 1.

The effect of intravenous and oral chlorpromazine therapy supplemented with paraldehyde given by mouth in a case of severe tetanus. The commencement of oral chlorpromazine therapy is denoted by the vertical line. "Major spasms" were those occurring spontaneously and lasting more than 15 seconds.

currently, it is impossible to evaluate the relative importance of each. Chlorpromazine alone failed to control the spasms entirely, but was satisfactory when given with paraldehyde. It may be that the two drugs are complementary in controlling spasms (Shanker and Mehrotra, 1959).

The patient's peculiar mental state during the period of convalescence, with polydipsia and polyuria, was an unusual feature and is placed on record. Depression, irritability and apathy after chlorpromazine therapy for tetanus were recorded by Packard *et alii* (1958).

It is hoped that this case report will encourage others to undertake the treatment of severe tetanus with chlorpromazine given by mouth and ancillary sedation, so reducing the call for aided respiration and intravenous therapy.

References.

- BENJAMIN, M. K. (1960), "Chlorpromazine in the Management of Tetanus: Report of a Case", *MED. J. AUSTR.*, 1: 976.
- LAURENCE, D. R., BERMAN, E., SCRAGG, J. N., and ADAMS, E. B. (1958), "A Clinical Trial of Chlorpromazine Against Barbiturates in Tetanus", *The Lancet*, 1: 987.
- PACKARD, R. S., CARTMILL, T. B., and HENRY, J. G. (1958), "Management of Severe Tetanus: Use of Chlorpromazine in Two Patients", *Brit. med. J.*, 1: 16.
- SHANKER, A., and MEHROTRA, L. S. (1959), "A Preliminary Report on Chlorpromazine in Tetanus", *Brit. med. J.*, 2: 1150.

Addendum.

A further patient suffering from severe tetanus, a man, aged 27 years, has been successfully treated in this unit by the same régime.

Reviews.

Gynecological Therapy. By J. Novak, M.D. 1960. New York, Toronto, London: McGraw-Hill Book Company Inc. 8½" x 5½", pp. 270, with illustrations. Price not stated.

It must be very difficult for a specialist in any particular field, or for a person who has held an academic post for many years, to write a book "primarily dedicated to the general practitioner", and if this is successfully accomplished, it shows a rare degree of *rapprochement* and knowledge of the way of life and the particular problems of the family doctor. We believe that this book has achieved the desired result and illustrates the point.

The book may be regarded as being broadly divided into two parts—first, a presentation of a list of disorders that may be responsible for the patient's predominating symptoms, and second, a discussion of therapeutic measures. However, by its being arranged in this way, we think that there is perhaps some loss of perspective. For instance, in the second chapter, the subject of amenorrhoea tends to become obscured by the detailed discussion of the various conditions associated with it—as, for example, the menopause. This sort of thing occurs in several places, but admittedly it is of little consequence in a review of clinical gynaecology. The important thing is that the facts are there and can readily be found by reference to a good index.

It is doubtful whether the very comprehensive and useful chapter on drug therapy, mainly devoted to the endocrines, would be used very much by the general practitioner, and the same could be said of the section on physiotherapy, much of which has a continental flavour and is not generally applicable to this country.

It is taken for granted that major gynaecological operations are not performed by general practitioners, and therefore technical details of these surgical procedures are omitted. Nevertheless, the applicability and efficiency, as well as the dangers, of these operations are given in the chapter entitled "The Essentials of Gynaecological Surgery", which contains much sound information. Likewise, very useful is the final chapter on female hygiene, which is comprehensive in its scope, yet extremely practical in approach.

The general tone of the book is conservative, and, while the nature of the presentation is somewhat different, the teaching of the important issues conforms generally to that of Australian medical schools. Within its pages there is no doubt a fund of valuable information, and the addition of a good index makes it a very handy reference book for general practitioners.

General Anaesthesia. Volumes 1 and 2, edited by Francis T. Evans, M.B., B.S., F.F.A.R.C.S., D.A., and Cecil Gray, M.D., F.F.A.R.C.S., D.A.; 1959. London: Butterworth & Co. (Publishers) Ltd. 9½" x 6½", pp. 574, with illustrations. Price: £9 18s.

With some books for review, it is possible to read the text completely and then pass judgement. The present book consists of two volumes, of some 431 and 531 pages respectively, and is much too large for detailed reading in the time available. One must then read the presentation of new subject matter and important topics, and make comparisons with previous editions and with similar books. These volumes replace "Modern Practice in Anaesthesia" and incorporate some topics from "Modern Trends in Anaesthesia".

The editors are aware that, with such diverse authorship (16 contributors—some old, some new), there is inevitable overlapping and some conflict of opinion on certain topics. Further, there is some separation of subject matter with no continuity, presumably to allow specialists in various fields to contribute. Both these characteristics are stated to be good for teaching; but the book fails to make a composite whole and allow the graduate student reader to comprehend the subject as he should. Some chapters from what can be considered the previous edition are presented with greater clarity and, in some instances, a refreshing brevity. "Anaesthesia in Diabetes" and "Anaesthesia in the Difficult Patient" are two such examples. However, the latter chapter is directed mainly to cardio-respiratory difficulties, and although Ludwig's angina is mentioned, it is not discussed. Further, it is not indexed and, after some searching, was found in "Anesthetic Emergencies".

The attempted scope of the work is extensive. There are some interesting and important presentations not usually found in ordinary anaesthetic textbooks. Local analgesia

has been intentionally omitted, except, for some obscure reason, in a few selected operations, and an incomplete chapter on anatomy is included. Graphs, tables and photographs are liberally used, some of the last-mentioned being redundant, and no direct reference is made to the source of some diagrams from another publisher. The volumes are well produced, the first consisting of basic principles, and the second of techniques, special fields and hazards.

The authors state that their aim was to produce a book suitable for study and reference. The foregoing criticism would suggest that the book is unnecessarily large and that the two aims are incompatible. It is believed that the post-graduate student would find it cumbersome as a book of study. It will no doubt become a reference book for all those interested in anaesthesia. The deficiency as a reference book is somewhat compensated for in that there is an extensive bibliography at the conclusion of each chapter.

Disc Lesions and Other Intervertebral Derangements Treated by Manipulation, Traction and Other Conservative Methods. By E. J. Crisp, M.D., F.Phys.Med.; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" x 5½", pp. 166, with 48 illustrations. Price: 15s.

THIS is a small book which covers in considerable detail the anatomy, pathology, signs, symptoms and treatment of numerous lesions of the spine. The section on anatomy is concise and covers the relevant structures very well. The pathology is discussed in considerable detail and is mostly extremely good. Some of it is rather theoretical, and some of the conditions described may or may not occur. A book of this type is usually purchased for the section on treatment, and here is a good system of treatment which should help the doctor who finds that his treatment of these patients tends to be rather haphazard.

On the whole, the book is good, and should be very helpful to the general practitioner who feels he would like to know more about the degenerative lesions of the spine. Some of the author's theories would not be universally accepted; but there is still much that must be discovered before all spinal lesions can be fully understood. Our one criticism of the book is that rather too much space is taken up in relating pathology to symptoms and signs, and the treatment and handling of these patients are not discussed in sufficient detail. We think that the people who read this book would be more interested in the practical aspects rather than in theories.

Fluid Balance in Obstetrics: A Critical Review. By Philip Rhodes, M.A., M.B., F.R.C.S. (England), M.R.C.O.G., 1960. London: Lloyd-Luke (Medical Books) Ltd. 8½" x 5½", pp. 180. Price: 25s.

IN this book Dr. Rhodes succeeds in his attempt to present his subject in a manner which clinicians can understand. The introductory chapter on physical chemistry recalls to the reader the essentials of osmosis and equivalent weights and clearly explains the modern terminology of milliequivalents. There is an excellent summary of water, sodium and potassium balance in the non-pregnant woman, with some reference to premenstrual tension. This is followed by a discussion on some of the physiological aspects of normal pregnancy—namely, weight gain, and water, sodium and potassium retention. The hormone balance of pregnancy is also discussed.

Water and salt depletion in pregnancy, with particular reference to hyperemesis gravidarum, is described, and a practical method of treatment is outlined. This is followed by the special problems associated with hydramnios, diabetes mellitus, hydrops fetalis, diabetes insipidus and Addison's disease. This particular chapter of the book will not be of interest to most clinicians, as the subjects dealt with are not common and are not of practical import.

The chapter on pre-eclampsia is a masterpiece, in that it critically reviews most of the experimental work that has been done on this condition, and from the natural history of the disease the author attempts to evaluate the changes which occur in the electrolytes. He concludes by stating that cell membrane permeability and the factors that control it would appear to be the key to solving the problem of toxæmia. He rightly states that control of weight gain in pregnancy will not influence the incidence of pre-eclampsia, neither will the use of hypotensive drugs. He discounts the use of diets of low salt content as treatment, and is not in favour of the prolonged use of diuretics. He believes, as we do, that the sheet anchor of treatment is rest in bed. His chapters on anuria, oliguria and the hemorrhages of obstetrics present summaries of current knowledge.

The book concludes with chapters on normal and prolonged labour, Caesarean section and the puerperium, in

each of which are logically presented principles of treatment by intravenous therapy which are helpful to the clinician and based on a sound biochemical basis.

This book should be in the library of every obstetrician and in hospitals where large numbers of patients are confined. It is essential that all graduates reading for higher degrees or diplomas should have a thorough knowledge of its contents.

Queensland Year Book, 1959. Number 20. Compiled by S. E. Solomon; 1959. Queensland: Commonwealth Bureau of Census and Statistics. 8½" x 5", pp. 472. Price: Not stated.

THE "Year Book" is a useful and well-produced summary of life, industry and trade in Queensland. We may quote a few of the facts from the chapter on population and health. Queensland has had a rapid growth of population, but still shows the marks of the low fertility rates in the 1930's, as do the other States. This indentation in the population pyramid has been partly filled out by migrants. Of the foreign-born, 93,000 were born in the British Isles, 17,000 in Italy, 7000 in Germany and 5000 in the Netherlands. The population is not so concentrated in the metropolis as in the other States, but there are a number of large provincial cities.

Addendum 1960 to the British Pharmacopoeia 1958. Published under the direction of the General Medical Council pursuant to the *Medical Act, 1956*; 1960. London: The Pharmaceutical Press. 9" x 5½", pp. 108. Price: 30s. (English).

THE first Addendum to the British Pharmacopoeia, 1958, was published on October 3, 1960, and becomes official in Great Britain from March 1, 1961. The several already published amendments to existing monographs which became official in September, 1958, and June, 1959, respectively, are incorporated in this, together with some 40 additional amendments—49 monographs on newly-added drugs and preparations, and several changes and additions in the appendices. Practically all the added drugs have been established in therapeutic use for a considerable time, while many other contemporary drugs of no less value have not been so favoured. The task of selection or rejection must be one of great difficulty and fine judgement.

One might have expected to see some of the newer antibiotics—antibacterial and fungistatic—or some synthetic modification of existing ones, such as penicillinase-resistant penicillins; but novobiocin is the only one admitted. It is presented in the form of its calcium and monosodium salts, and is formulated for presentation as tablets having a dose equivalent to 1 gramme of novobiocin a day. Potassium and calcium salts of phenoxymethylpenicillin are added, and the monograph on phenoxymethylpenicillin tablets is revised to include these as well as the free acid.

Of the many non-mercurial diuretics that have come to occupy so prominent a place in conditions of hypertension and cardiac failure, the only representative is chlorothiazide, whose popularity is receding in favour of more recent modifications.

Among the immunological products are the Salk vaccine—an inactivated trivalent poliomyelitis prophylactic—and the mixed vaccines of diphtheria with tetanus, and typhoid A and B with cholera. Monographs on the Bacillus Calmette-Guérin vaccine and on smallpox vaccine include dry forms in addition to the liquid forms.

Hormones are represented in a revised monograph on corticotrophin and two others on prolonged-action corticosteroids having gelatin and zinc hydroxide respectively as the action-delaying additives. The current drugs for hypothyroidism are reinforced by the addition of the sodium salt of triiodothyronine, officially lyothyronine sodium, with doses quoted as 5 to 200 µg. per day. On the other hand, potassium perchlorate with a controlling dose of 1 gramme per day, tapering to a daily maintenance dose of 200 to 500 mg., is included for thyrotoxicosis. Tolbutamide is the first of the hypoglycæmic drugs for oral administration to gain entry.

In view of the present-day clamour for ataractic drugs, it is surprising that chlorpromazine and reserpine of the current B.P. should still remain the only representatives, while, to the already large and versatile group of barbiturates, amylobarbitone sodium is added. Possibly as a reaction to the increasing use and perhaps misuse of barbiturates, another barbiturate antagonist and analeptic, bemegride, is now introduced.

In response to the increasing use of vitamin K₃, natural or synthetic, as opposed to its many simpler homologues and

modifications, this drug now makes its pharmacopoeial debut as phytomenadione for administration in the form of capsules and as an intravenous injection, the water-insoluble oily vitamin being dispensed in water for injection with suitable emulgators and stabilizing agents.

From the increasing group of cytotoxic drugs, two anti-leukemic representatives, busulphan and mercaptopurine, have been chosen.

Among other drugs finding a place in the Addendum are hydroxychloroquine, of which doses are quoted for the treatment of discoid lupus erythematosus, rheumatoid arthritis and giardiasis in addition to its primary application to malaria; probenecid as a uricosuric agent, and as an adjunct to penicillin and paraaminosalicylate treatment for its maintenance of blood levels; the fluorinated hydrocarbon, halothane, as a general anesthetic; the cholinesterase inhibitor, pyridostigmine bromide, for particular application to myasthenia gravis and as an antidote to curare-like drugs; and chlorhexidine hydrochloride, together with its 20% digluconate solution, as potent antibacterial agents.

The various amendments to existing monographs and changes in the appendices are of greater interest to the pharmacist than to the physician.

The Development of the Infant and Young Child: Normal and Abnormal. By R. S. Illingsworth, M.D., Leeds, F.R.C.P., D.P.H., D.C.H.; 1960. Edinburgh and London: E. & S. Livingstone Ltd. 8½" x 5½", pp 326, with 95 illustrations. Price: 27s. 3d. (English).

This volume is the paediatrician's rather than the psychologist's approach to the subject. In it, Professor Illingsworth, who acknowledges the profession's debt to Gesell, treats of the mental development of the child, and does so by assessment of "the physical and environmental factors and a detailed developmental history".

The early chapters consider such subjects as the predictive value of developmental assessment, environmental factors and development, and associations of physical defects and disease with mental development. While the book contains nothing new, the critical survey of the literature and the encompassment of a scattered field in short space are a remarkable and valuable achievement. The author's discussion of normal development contains no iconoclasm, and rightly emphasizes the variations which can exist in the normal child. The biographies cited are well chosen to illustrate this point. The section on history-taking is excellent and detailed, the section on "Examination of the Child" gives details of the techniques he uses; this is of great value to all interested in the child.

In general, this book achieves its purpose; it is important and timely in view of the growing practice of the "well-child" conference, and the shift of pediatric interest from the ill child to the healthy child. Not the least important aspect of this publication is the excellent (and critical) bibliography given. The sections on history-taking and examination will be welcomed by all in their approach to the normal or abnormal child. The clarity of type and illustrations presented is beyond reproach.

Atlas and Manual of Dermatology and Venereology. By Professor Dr. W. Burdckhardt; translated and edited by Stephan Epstein, M.D.; 1959. London: Baillière, Tindall and Cox. 9½" x 6½", pp. 294 with illustrations. Price: 112s. (English).

This atlas and manual contains 99 colour plates and 73 black-and-white illustrations. The 99 colour plates are indeed the finest that we have seen in this type of publication.

The letterpress is directed to the concise presentation of the commonly occurring skin diseases for, as the translating editor points out, non-dermatologists. Some of the rarer conditions are presented in synopses, though not illustrated. One wonders whether it would not have been better to omit these and be satisfied with those thought worthy of full treatment. This, of course, brings up the question as to the future of the dermatological atlas. Who uses an atlas? Does the general practitioner use it as a mariner does a chart when sailing in strange waters? An inquiry amongst readers would be of interest. The number of atlases sold by medical booksellers in Sydney does not indicate a great demand. Perhaps the provision of colour transparency sets will replace them in the future.

However, this book is a manual as well as an atlas. The comments are useful and succinct. The methods of treatment suggested are common-sense and up to date, and do not confuse the reader with long lists of alternatives. It is recommended.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"Progress in Endocrinology, Part II: Biochemistry and Biological Actions of Steroids and Other Hormones", Memoirs of the Society for Endocrinology, No. 10, edited by K. Fotherby, J. A. Loraine, J. A. Strong and P. Eckstein; 1961. Cambridge University Press. 9½" x 7½", pp. 180. Price: 45s. net (English).

"The Chemistry of Heart Failure", by W. C. Holland, M.D., and R. L. Klein, Ph.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd.; Toronto: The Ryerson Press. 9" x 6", pp. 128. Price: 44s. (English).

"The Pathology of Cerebral Palsy", by A. Towbin, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications, 1961. 9" x 6", pp. 216 with illustrations. Price: 64s. (English).

"The Tutoring of Brain-Injured Mentally Retarded Children", by J. J. Gallagher, Ph.D., with a foreword by S. A. Kirk, Ph.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" x 6", pp. 210. Price: 54s. (English).

"Hearing Enhancement", by J. A. Victoreen, LL.D., with a foreword by F. S. Forman, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications, 1961. 9" x 6", pp. 196. Price: 60s. (English).

"Quantitative Cellular Hematology", by J. M. Yoffey, D.Sc., M.D., F.R.C.S. (Eng.); 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd. 9" x 6", pp. 136 with illustrations. Price: 44s. (English).

"Adrenergic Mechanisms: A Ciba Foundation Symposium", edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and M. O'Connor, B.A.; 1960. London: J. & A. Churchill Ltd. 8" x 5½" pp. 652 with illustrations. Price: 70s. (English).

"Metabolic Effects of Adrenal Hormones: Ciba Foundation Study Group No. 6", edited by G. E. W. Wolstenholme, O.B.E., M.A., M.B., M.R.C.P., and M. O'Connor, B.A.; 1960. London: J. and A. Churchill Ltd. 7½" x 5", pp. 118 with figures. Price: 12s. 6d. (English).

"Studie Over De Achromatische Gezichtsfuncties In De Congenitale Sensoriele Anomalieën Van Het Menselijk Oog En Bij Sommige Amphibia En Reptilia", by Dr. Guy Verriest, with a foreword by Professor Dr. J. François; 1960. Brussels: Arsia Uitgaven N. V.; The Hague: Uitgeverij Dr. W. Junk. 9½" x 6½", pp. 480 with a few illustrations. Price not stated.

"Bleeding Syndromes: A Clinical Manual", by O. D. Ratnoff, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd.; Toronto: The Ryerson Press. 9" x 6", pp. 298. Price: 68s. (English).

"The Surgical Treatment of Portal Hypertension, Bleeding Esophageal Varices and Ascites", by M. J. Mackay, M.D., D.A.B.S., F.I.C.S., with a foreword by Emile Holman, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd.; Toronto: The Ryerson Press. 10" x 6½", pp. 268 with illustrations. Price: 84s. (English).

"The Transplantation of Tissues and Organs", by M. F. A. Woodruff, M.D., M.S. (Melb.), F.R.C.S., F.R.C.S.E., F.R.A.C.S.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications; Toronto: The Ryerson Press. 10" x 6½", pp. 314 with illustrations. Price: £10 4s. (English).

"Evaluation and Management of the Brain-Damaged Patient", by J. S. Tobis, M.D., and M. Lowenthal, M.D.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications; Toronto: The Ryerson Press. 9" x 6", pp. 120 with illustrations. Price: 48s. (English).

"The Chemistry of Immunity in Health and Disease", by D. W. Talmage, M.D., and J. R. Cann, Ph.D.; 1961. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications; Toronto: The Ryerson Press. 9" x 6", pp. 190 with a few illustrations. Price: 46s. (English).

"Introduction to Biochemistry", by E. O'F. Walsh, B.Sc., Ph.D., F.P.S., F.R.I.C.; 1961. London: The Universities Press Ltd. 8½" x 5½", pp. 262. Price: 51s. 3d.

"The Chemical Basis of Clinical Psychiatry", by A. Hoffer, M.D., and H. Osmond, M.R.C.S., D.P.M.; 1960. Springfield, Illinois: Charles C. Thomas; Oxford: Blackwell Scientific Publications Ltd.; Toronto: The Ryerson Press. 9" x 5½", pp. 292. Price: 68s. (English).

The Medical Journal of Australia

SATURDAY, APRIL 29, 1961.

THE PLUNKET SOCIETY.

THE Plunket Society in New Zealand recently celebrated its Golden Jubilee, and in July, 1960, the Prime Minister of New Zealand, on behalf of the Government, reaffirmed the mandate given to the Society in 1907, a mandate making it responsible for the provision of an infant welfare service. Officially designated the Royal New Zealand Society for the Health of Women and Children, the Society is still known throughout New Zealand (and elsewhere) by its shorter title, which honours the great interest taken in its work in the early days by the Governor-General of the Dominion, Lord Plunket, and Lady Plunket. The founder was, of course, Sir Truby King. He, from his observations in the successful rearing of animals on the farm of Seacliff Mental Hospital, of which he was medical superintendent, became convinced that the same success would result from the application of the principles used to infant welfare work. He therefore set himself to enlist the aid of the women of New Zealand, telling them of the simple and natural essentials for good health. In response to his request that they form a voluntary society "to help the mothers and save the babies", the Plunket Society came into being at a public meeting in Dunedin Town Hall in May, 1907. The story of its growth from that time and its present extensive activities have been set out in a recent attractive publication issued by the Society.¹

The essence of the work of the Plunket Society is that it is a community health activity. "For the community by the community" is the constant motto. A democratic organization, it has 104 branches and 530 sub-branches throughout New Zealand. Through their delegates to Provincial Conferences the members of the Society's national body, the Dominion Council, are elected. Policy is determined by Dominion General Conferences held every second year, to which all Branches may send delegates. The Dominion Council, which meets twice a year, delegates most of its day-to-day activities to the Dominion Executive. The executive officers of the Society are the Director of Medical Services, the Director of Nursing Services and the Dominion Secretary.

It is interesting to note that the Director of Medical Services, who is broadly responsible for the teaching and

methods advocated by the Society, has important and far-reaching contacts within the medical profession: he is chairman of the Medical Advisory Committee of the Society, which is widely representative; he is currently an office-bearer of the New Zealand Paediatric Society, and is on the Executive of the New Zealand Branch of the British Medical Association; he conducts a limited paediatric consulting practice, and is lecturer in paediatrics at the Otago Medical School, which permits him to coordinate the training which is given to Plunket nurses with that given to medical students.

The Director of Nursing Services is responsible for the training, deployment and work of the 250 Plunket nurses, and, through the Karitane hospital matrons, for the training of the Karitane nurses, which takes place at the Karitane hospitals. Of these there are six situated in the large metropolitan areas (Auckland, Wanganui, Wellington, Christchurch, Dunedin, Invercargill), each with its own area of support. Registered as private medical hospitals, they have an honorary staff of local doctors chosen for their special knowledge of paediatrics. The nursing staff consists of the matron and trained staff, together with trainees on the basis of one trainee to each child. The work of the hospitals is divided into four sections: the premature section, mother and premature child usually coming to the Karitane hospital at about the tenth day; the general section, for bigger babies with some special problem who are recommended for admission by a medical practitioner; the toddler section, for pre-school children with various problems; the mothercraft section, for mothers with some special problem of feeding or management of the baby.

The two distinct types of nurse, the Plunket nurse and the Karitane nurse, make up the essential field force of the Society's work. The Plunket nurses' training consists of a four-months post-graduate course for registered nurses and is held at the Dominion Training Centre at Dunedin. They are nurses of some seniority, who not only have State registration but are experienced in maternity nursing or midwifery. The special training, the emphasis in which is on practical aspects, is modern, orthodox paediatrics. The work of the Plunket nurse is primarily health promotion and health supervision in the infant and pre-school groups, and is carried on through visits to the home at the mother's invitation, through local Plunket clinics to which the mothers bring their children, and through information and lectures given to various special groups, especially Mothers' Clubs, which are an important adjunct to the Plunket Society's work and number about 250.

Karitane nurses are trained at all six Karitane hospitals. They are usually young girls who have just left secondary school. After sixteen months' practical and theoretical training in the Karitane hospitals, they do four months' "casing" in a private home before they can obtain their Karitane infant nursing certificate. After qualifying, they work in private homes, either giving help and support to a mother with her baby, or caring for a family when the mother is in hospital. A few are employed in maternity hospitals or in children's wards.

The Plunket Society has flourished in New Zealand since its inception, and its Karitane methods have been

¹ "The Plunket Society": 1961. Dunedin: The Royal New Zealand Society for the Health of Women and Children (Inc.). 9½" x 7½", pp. 24.

widely accepted also in Australia. There is every indication that it will continue to flourish. It has developed and worked along its own lines and is a standing memorial to the man of vision who founded it. Not all of Sir Truby King's ideas have stood the test of time, but the Plunket Society most certainly has, and it has a good deal to teach all who are concerned with infant welfare. Of even wider interest is the emphasis which it has placed from the beginning on community self-help and on the democratic organization which we have already described. The branch and sub-branch committees play a very active part in the Society's work; they join in the promotion of health education, by fostering Mothers' Clubs, by acting on special committees such as hydatid committees, accident prevention committees and mental health committees, and by encouraging young mothers to use the Plunket service; they organize voluntary labour to build Plunket clinics and flats for the Plunket nurses, they buy and maintain vehicles for the nurses, and they decorate, paint and clean the clinics; they raise money for the Society in substantial sums, which successive Governments have subsidized. This is an interesting picture, which calls for the highest commendation. Perhaps the most important thing about it is that it shows a strong spirit of community responsibility and self-help in a country which we have come to think of as much more advanced in the ways of the Welfare State than ourselves. Have we anything of the same calibre to offer?

Current Comment.

THE TREATMENT OF SEVERE TETANUS.

WE wish to call attention to a statement on the early management of severe tetanus by I. J. Wood and I. R. Mackay of the Clinical Research Unit of the Royal Melbourne Hospital on page 634 of this issue. This is amplified by a case report from the same centre on page 625. The last ten years have seen the treatment of severe tetanus metamorphose from a policy of watchful expectancy to one of active management, in which the clinician aims to be in complete control of his patient throughout his illness. It has been a period of trial and development, with considerable divergencies in policy from centre to centre. We think that most authorities on the subject would now agree with the proposition that severe tetanus should whenever possible be treated in major centres, fully equipped and staffed to carry out the elaborate régime described in this issue by B. S. Clifton (page 618) in a paper from the Royal Prince Alfred Hospital, Sydney. However, as stated by Wood and Mackay, it is still controversial whether maintenance treatment of tetanus should be with relaxant drugs and assisted respiration, or whether an attempt should be made to maintain such patients on a régime such as that found successful in Melbourne. The difference of opinion is not fundamental, as in both régimes an initial attempt is made to control the patient by sedation alone. The question resolves itself into one of how far sedation should be pushed before recourse is had to curarization and artificially controlled or assisted respiration. It may be noticed in passing that R. S. Packard¹ and his colleagues described the successful treatment of two patients with severe tetanus by sedation with chlorpromazine and amylobarbitone three years ago at the Royal Prince Alfred Hospital. At the end of their paper they mention that

three further patients with severe tetanus had been successfully treated by the same régime, and the implication is that most cases even of severe tetanus should be amenable to such treatment. As there appears to be no prospect that the supply of tetanus patients will dry up, it will be interesting to see in due course statistics as to the proportion of patients whom it is found necessary to control by curarization and artificial respiration at the various centres. It is quite possible that new drugs will appear which will make it possible to control spasm in all cases without recourse to curarization. Failing this, it seems probable that at all centres there will be found an irreducible core of severe cases in which management by curarization and artificial respiration as described by Clifton is necessary.

It is interesting to compare these views with those put forward in a recent American paper on the same subject by M. A. Perlstein of Cook County Hospital, Chicago, and his colleagues.² For these authors the problem is complicated by the fact, fortunately not significant in Australia, that a large proportion of their adult patients are heroin addicts, among whom tetanus occurs in a particularly severe form, with a mortality rate of about 70%. Perhaps the most noteworthy feature of the régime described by Perlstein and his colleagues is that, unlike most recent writers on the subject, for whom chlorpromazine is the sheet anchor of their sedative régime, they use meprobamate, administered intramuscularly, as their first line of defence for the control of seizures. They state that in their experience it has proved an astonishingly good antispasmodic drug in tetanus, and that it effectively abolishes seizures which are triggered by somatic stimuli such as pinpricks, loud noises or flashing lights. However, it does not affect seizures triggered by visceral stimuli or by proprioceptive stimuli (e.g., turning the patient). They therefore consider that the persistence of seizures after the administration of meprobamate should call for a search for a visceral cause, such as a distended bladder, faecal impaction or mucus in the tracheo-bronchial tree. Only when meprobamate by itself is inadequate do they use chlorpromazine in moderate doses (25 to 50 mg. given intramuscularly every three or four hours) as an adjuvant, but they consider it to have an undesirable depressing and soporific effect and, when administered over a prolonged period, to tend to lower the blood pressure to a dangerous degree. For this reason they recommend the addition of 10 to 25 mg. of promethazine hydrochloride to each dose of chlorpromazine. When even this combination is not effective barbiturates may be given as well, but they are used only sparingly. In intractable cases, artificially controlled respiration is used, but the impression is given that this is not often necessary. An incidental advantage of the use of meprobamate is that the intramuscular injection of quite large volumes appears to be virtually painless, apparently owing to some local analgesic action of meprobamate. As in most modern régimes for the treatment of severe tetanus, tracheostomy is the rule, but at the Cook County Hospital this is performed under local anaesthesia. Nutrition is maintained by fluids administered intravenously "for the first 12 to 24 hours, and even longer if deemed advisable". Thereafter the patient is fed by a naso-gastric tube until he is well enough to swallow. For patients who cannot urinate spontaneously, Perlstein and his colleagues recommend catheterization every six to eight hours; they state that an indwelling catheter in severely affected patients almost invariably triggers continuous severe seizures. For the rare cases in which catheterization is necessary for more than a short period, they suggest that a suprapubic cystostomy should be considered. Finally, Perlstein and his colleagues describe the special measures necessary for their patients who are heroin addicts; in these cases they are experimenting with the use of hypothermia in an attempt to reduce the metabolic needs of the patients and the rate of growth of secondary inflammatory organisms. They state that the use of hypothermia has definitely decreased morbidity and increased survival time, but that so far it has not greatly affected the mortality rate.

¹ Brit. med. J., 1958, 1: 16 (January).

² J. Amer. med. Ass., 1960, 173: 1536 (August 6).

SPENT RADON SEEDS.

The history of medical usage of ionizing radiation is replete with practices that were at first regarded as innocuous but subsequently proved hazardous.

This sentence is quoted from the concluding paragraph of a paper by J. B. Graham and his colleagues,¹ in which they draw attention to the residual activity and possible late effects of "spent" radon seeds which have remained *in situ*. Radon, or radium emanation, is a gaseous radioactive element which gives out the same radiations as radium, but has a brief half-life of 3.8 days, and degenerates into radium C, D and E. All these forms are radioactive, and radium D has a half-life of 19 years, but this residual activity has been regarded as of no consequence because it is mainly alpha or beta radiation, and so usually does not escape through the gold sheath of the radon seed. Graham and his colleagues point out that these unique properties were early recognized and led to the use of radon almost from the beginning of radiotherapy. Because of radon's short half-life and the belief that the residual radioactivity was negligible, radon seeds were widely used in situations where they would be permanently implanted, and it was considered unnecessary to make any attempt to remove them subsequently. The results were satisfactory, and there was no reason to believe that patients treated in this way were any more prone to late complications than those given other forms of radiotherapy.

The possibility that spent radon seeds might not be completely innocuous occurred to Graham and his colleagues when, in a three-months period, they encountered one vesico-cervical fistula, apparently due to radiation, 19 years after the insertion of radon seeds for cancer of the cervix, and three recurrences of tumour at intervals of 12, 20 and 21 years after the implantation of radon seeds in the cervix. They point out that late recurrences after radiotherapy for cancer of the cervix are uncommon, and that recurrence after 15 years is "distinctly rare". Late radiation complications are equally rare. On investigation it was found that all of these patients had detectable radiation from the retained seeds, active enough to be measured by simple scanning techniques. Graham *et alii* got their colleagues in the nuclear medicine department to scan 18 patients who had had seeds implanted between 1930 and 1947, with a scintillation counter such as is used to measure ¹³¹I uptake in the thyroid. It was found that all but three exhibited pelvic radiation ranging from 16% to 137% above background. In another paper in the same journal,² H. E. Johns and L. D. Skarsgard describe their investigation of this residual radioactivity. They showed that the beta rays emitted by radium E strike the gold and generate a continuous spectrum of X radiation with peaks at 70 kev and 167 kev. These X rays are of a very low intensity, but Graham *et alii* point out that the evaluation of this dose in terms of conventional exposures is confused by two considerations. In the first place, the tissues were heavily irradiated at the beginning, and so may not respond as normal tissue would do to this amount of radiation; secondly, the radiation has been maintained over many years at a fairly constant rate. Examination of vaginal smears from patients with old radon seeds showed that the exfoliated cells in these cases presented a unique appearance, with large cells and abnormal nuclei, reminiscent of that seen in cases of carcinoma-in-situ. When these were compared with smears from patients treated by radium and X rays during the same period, it was found that the latter had a much lower incidence of cellular abnormality. On the other hand Graham and his colleagues point out that radon seeds are apparently tolerated by the tissues for long periods of time, and that they have been able to find only one report to the contrary, namely an account of a case in which ulceration and discharge of seeds occurred 20 years after they had been implanted in the skin. No mention is made in this report of residual radioactivity.

We agree that it is important not to exaggerate the hazards of the medical use of ionizing radiation, and that there is a danger of causing an exaggerated timidity about their use, but Graham and his colleagues do seem to have raised an important issue, one which, in their own words, "would bear more thorough investigation".

INCREASING INTEREST IN CHILD DEVELOPMENT.

The last decade or so has seen a quickening interest in the study of child development, undoubtedly stimulated by the demands of an increasing number of parents for guidance in child rearing and by the changing attitude towards the handicapped child. Although these two reasons seem widely apart, they both depend upon a sound knowledge of child development. Parents want to know what to expect of their children at different ages, both to ensure the provision of adequate stimulation and to prevent making unrealistic demands. It is now recognized that an attempt should be made to diagnose the handicapped child as early as possible in order that his special needs may be met; this applies particularly to the mentally retarded child.

Some confusion still exists about the scope and limits covered by the title "child development". Ausubel has defined it as "a branch of knowledge concerned with the nature and regulation of significant structural, functional and behavioural changes occurring in children as they advance in age and maturity". Child development is thus more than a description of the characteristics of children at different ages, since it also covers the study of how the transformation from one stage to the next occurs and the factors responsible for this. Furthermore, the interaction between the organism and the environment is an integral component of the study of child development.

Some have felt that the line of demarcation between child development and child psychology is not sufficiently clearly drawn. From the definition it is apparent that child development covers a much wider field than child psychology, attempting to bridge a number of disciplines, including genetics, embryology, education, sociology, paediatrics and psychiatry, whereas child psychology tends to concentrate on one phase of the child—behaviour and the conscious processes.

From the observations on many individuals, a number of investigators have built pictures of the patterns of development throughout childhood. From this they have prepared cameos of the characteristics at various ages as guides to doctors, nurses, teachers and others who want to assess the stage a child has reached. One recent accession to this list of schedules is a small pamphlet compiled by Dr. Mary Sheridan and issued by the British Ministry of Health.¹ In this the developmental characteristics of children are presented in four sections: posture and large movements, vision and small movements, hearing and speech, social play and behaviour. The combination of vision and small movements covers the activities listed by Gesell under the heading of adaptive behaviour. The expected achievements and behaviour at the ages of one, three, six, nine, 12, 15 and 18 months, and at two and a half, three, four and five years are given in tabular form. The lists are comprehensive, although it is not to be expected that every child will demonstrate his full capacities in respect of every item at one observation. The author of this pamphlet emphasizes that the results apply to the day on which the tests are made, and that a number of transient events can influence activity and behaviour; for example, performance in a young child is often below his normal capacity in the prodromal stages of an illness. The pamphlet presents a wealth of material within its 10 pages, and should prove of great value to the paediatrician and family doctor interested in the growth and development of the children in his care.

¹ *Radiology*, 1960, 74: 399 (March).

² *Ibidem*, 1960, 74: 403 (March).

¹ "The Developmental Progress of Infants and Young Children", by Mary S. Sheridan; 1960, London: H. M. Stationery Office. Price: 1s. 3d.

Abstracts from Medical Literature.

SURGERY.

Carcinoma of the Breast.

R. J. UTZSCHNEIDER AND J. C. MCCANN (*New Engl. J. Med.*, November 3, 1960) present the results obtained in 245 patients with carcinoma of the breast seen at a community hospital in Massachusetts in the years 1946 to 1954. They obtained a 100% follow-up. The primary operability rate was 83%; 176 patients underwent radical mastectomy, with 5 deaths in the post-operative period, and 28 underwent simple mastectomy. The over-all five-year survival rate after radical mastectomy was 66%, and the ten-year rate was 45%. The authors present a table showing comparable results both from large medical centres and from smaller community hospitals. They conclude from this that the "classic" standard radical mastectomy is a technique which will provide comparable results throughout the country both in the large centres and in the community hospitals. They conclude that it becomes more and more evident that the inherent nature of the disease will require new modalities of treatment, rather than improvement in the technique of the standard radical procedure, to achieve more favourable results.

Wookey Operation for Carcinoma of the Hypopharynx.

R. A. MUSTARD (*Surg. Gynec. Obstet.*, November, 1960) discusses the use of the Wookey operation for carcinoma of the hypopharynx and the cervical part of the oesophagus in the light of 44 cases in which the operation was performed at Toronto General Hospital. These include 30 patients operated on by Wookey (including his original case) and 14 operations by the author. The operation is a two-stage procedure. At the first operation a transversely placed, full-thickness skin flap is fashioned, the involved tissue is then excised (usually the larynx, pharynx and upper cervical part of the oesophagus, less commonly the cervical part of the oesophagus only), and the flap is used to construct a deep, skin-lined groove connecting the pharynx above and the oesophagus below. At the second operation 6 to 12 weeks later, the groove is converted into a skin tube; in the author's experience direct closure of the resulting skin defect is almost always possible. Swallowing is allowed as soon as healing has occurred, and a full diet is soon possible. The author states that the cosmetic result is remarkably good. Of the present series of 44 cases, in 29 the larynx and "pharyngo-oesophagus" were excised, in 15 the larynx was spared. There were six operative deaths. There have been nine five-year survivors out of 37 patients operated on before January, 1955. The author states that the Wookey operation is applicable to only a limited group of tumours whose treatment necessitates the excision of a long segment of pharynx and oesophagus.

Indications are given for the selection of cases and the operative technique is briefly described, with notes on the pre-operative and post-operative management. The author states that no good solution has been found to the problem of hair growth in the reconstructed skin-tube oesophagus; in one patient, for whom hair growth was troublesome in the early years after operation, this difficulty ultimately resolved itself spontaneously, apparently as a result of natural adaptation, and there was no evidence of hair growth in the tube seven years later. Two long-term survivors who underwent laryngo-pharyngectomy have good pharyngeal speech, and the author recommends that the aid of a speech therapist should be sought as soon as the operations are successfully completed. The published results of two other centres (Cardiff and London) are shown to be comparable with those described in the present report. The results of radiation therapy are briefly discussed, and a short account is given of alternative surgical procedures which have as their objective the immediate reconstruction of the cervical part of the oesophagus at the time of excision. The author finally concludes that, in cases of carcinoma of the hypopharynx or cervical part of the oesophagus which are suitable for operation, excision offers the best chance for prolonged survival, and that until some method of one-stage reconstruction of the cervical part of the oesophagus becomes clearly established the Wookey procedure remains the safest and best.

Portacaval Shunt for Patients with Cirrhosis and Ascites.

H. G. BARKER AND K. REEMTSMA (*Surgery*, July, 1960) discuss fifteen patients with cirrhosis of the liver and "medically irreversible" ascites, who had been subjected to portacaval shunting. These patients constituted a high risk series from the standpoint of liver function and four did not live beyond 60 days. Failure to cure ascites occurred in two instances. The authors consider that nine patients experienced successful cure of their ascites, and they mention that five of these are still living, from four to six years after operation, completely free of ascites. All of these nine patients had undergone end-to-side shunts. They conclude that end-to-side portacaval shunting cures ascites in cirrhosis of the liver.

Acute Sigmoid Volvulus.

T. DRAPANAS AND J. D. STEWART (*Amer. J. Surg.*, January, 1961) discuss the surgical treatment of volvulus of the sigmoid colon, a condition which, they state, appears to be increasing in frequency. Considerable controversy exists concerning management of the acute episode, some surgeons believing that non-operative methods with use of the sigmoidoscope and rectal tube carry the risk of perforation, or of failure to recognize the presence of gangrenous bowel. A series of 40 patients, with a total of 116 episodes of acute sigmoid volvulus, has been studied by the authors. In 98 episodes an attempt was made to achieve reduction of the volvulus through the sigmoidoscope. Successful decompression was achieved in 82, with one

fatality. The one death in this group occurred shortly after sigmoidoscopy as a result of acute myocardial infarction. Perforation of the bowel did not occur in any patient. Laparotomy and detorsion of the twisted loop were performed in ten episodes, with three post-operative deaths, and primary resection in eight patients with four deaths. The authors conclude that sigmoidoscopy and insertion of a rectal tube is an effective procedure with practically no complications and that primary resection should be abandoned except in the presence of a strangulated volvulus. An analysis of the recurrence rate reveals that 60% of patients had two or more episodes of volvulus requiring treatment, and this suggests that elective resection of the redundant colon should be considered after relief of the emergency by conservative means.

Opacifying Gall-Stones.

D. H. WATKINS AND E. SALSAMAN (*A.M.A. Arch. Surg.*, June, 1960) discuss biliary calculography, which they describe as a procedure to identify opacifying gall-stones by prolonged administration of an oral cholecystographic contrast medium. The four-day "Telepaque" test fulfils the condition of prolonged preparation. They consider that the vast majority of bile duct calculi may be identified by this method, although a larger experience is required for accurate evaluation. They consider that biliary calculography is probably the most useful procedure to demonstrate bile duct calculi in the presence of jaundice and to show calculi within the intra-hepatic ducts. However, it is pointed out that all methods fail to visualize the ducts or identify bile duct calculi in the patient with a high degree of bile duct obstruction or liver insufficiency.

Ice Water as First-Aid Treatment of Burns.

A. G. SHULMAN (*J. Amer. med. Ass.*, August 27, 1960) states that personal experience first led him to use immersion in ice water as first-aid treatment for burns. Since then he has treated 150 patients with burns of all degrees, involving less than 20% of the body surface, by this method. The burned area is immediately immersed in a large basin of cold tap-water, to which ice cubes and hexachlorophene are added. The ice cubes melt quickly, and must be continuously replaced. In practice the temperature of the water varies between 41° and 55° F. When immersion is not practicable, cold wet towels are applied to the burned area. The author points out that the time factor is important and that this treatment should, if possible, be initiated by the patient or first-aid attendant at once. A striking feature of the treatment is the instant relief of pain; immersion is continued until the pain no longer returns on removal of the burned part from the cold water. This may take from 30 minutes to as long as five hours. The author's experience suggests that ice-water therapy will reduce the usual inflammatory process secondary to the burn. The visible area of erythema becomes obviously reduced while the cold is applied and does not reappear

later
be r
encou
one h
out th
burn
for m
to eva
only v
to sev
to the

Str
F. 2
discus
hernia
presen
are el
The le
men, i
age of
the yo
author
small
nerve
pathog
hernia
of this
bowel
nerve
operati
simple
treatm
pubic r
Henry,
verse i
pre-op
hernias
of the
is a hi
viable
common
patient

The
L. M
(Surge
manage
intestin
oesopha
Weiss
which
bout.
should
massive
hemorrh
whom t
at oper
mucosal
oesopha
gastroc
exerted
stomach
can be c
tions.
before b
upper g
Preven
Cell

G. O
Surg., J
ficient
danger
developi
cells dur
may de
needle t
readily
animals.

later; the extent of blistering may also be reduced. No infection has been encountered in patients treated within one hour of injury. The author points out that the beneficial effect of cold in burns has been sporadically advocated for many years, but that serious attempts to evaluate its usefulness have been made only within the last five years, and refers to several of the principal contributions to the subject.

Strangulated Obturator Hernia.

F. A. ROGERS (*Surgery*, August, 1960) discusses a series of 12 cases of obturator hernia, in 10 of which strangulation was present. The majority of such patients are elderly, weak and often emaciated. The lesion is more common in women than men, in a ratio of six to one. The average age of the patients was over 70 years, the youngest being 37 years of age. The author points out that the knowledge that small bowel obstruction plus obturator nerve pain (Howship-Romberg sign) is pathognomonic of strangulated obturator hernia should permit of the early diagnosis of this condition before gangrene of the bowel sets in. Unfortunately, obturator nerve pain is not always present. Early operation with release of the bowel and simple closure of the defect is the best treatment. The author prefers the suprapubic retroperitoneal approach of Cheatle-Henry, with either a vertical or a transverse incision, if the diagnosis is made pre-operatively. The majority of these hernias are right-sided and contain some of the terminal part of the ileum. There is a high incidence of strangulated non-viable bowel and a Richter type hernia is common. In this series, there were two patients with bilateral obturator hernias.

The Mallory-Weiss Syndrome.

L. N. STAHLGREN AND C. S. LING (*Surgery*, August, 1960) discuss the surgical management of massive upper gastrointestinal haemorrhage due to cardio-oesophageal mucosal lacerations (Mallory-Weiss syndrome) and report a case in which this occurred after an alcoholic bout. They state that this syndrome should be considered in any patient with massive upper gastro-intestinal tract haemorrhage preceded by retching, in whom the bleeding lesion cannot be found at operation. They point out that the mucosal laceration is situated near the oesophageal junction and is found by gastrotomy, downward traction being exerted on the posterior wall of the stomach through the opening. Bleeding can be controlled by suture of the lacerations. This syndrome must be excluded before blind gastrectomy is performed for upper gastro-intestinal haemorrhages.

Prevention of Implantation of Cancer Cells by Irrigation with Anti-Cancer Agents.

G. O. McDONALD *et alii* (*Amer. J. Surg.*, January, 1961) state that insufficient attention has been given to the danger of local recurrences of growth developing from implantation of malignant cells during operation. Such recurrences may develop at an anastomosis, in a needle track or in a scar, and can be readily produced experimentally in animals. The authors have used the

Walker 256 carcinosarcoma in female albino rats to test 25 chemicals for their efficacy in destroying implanted malignant cells. It was found that nitrogen mustard, in a dilution of 1 to 2 mg. per 100 ml., and sodium hypochlorite in 0.5% solution, buffered to pH 9.0, were about equal in efficiency. "Chlorpactin" was effective when used in 2% solution, but this concentration was too strong for wound healing. Since nitrogen mustard cannot be used in the wound if it is being used in systemic treatment, the authors have adopted the use of 0.5% sodium hypochlorite solution as an irrigant at the end of operations for cancer. They believe the irrigation should extend over a period of about four minutes. The method of preparation of the solution and the technique of wound irrigation are detailed in the paper.

Intestinal Antisepsis and the Spread of Tumours of the Colon.

I. COHN AND M. ATIK (*Amer. J. Surg.*, January, 1961) have used the Brown-Pearce tumour in the rabbit to study the fate of free tumour cells in the lumen of the colon. It had previously been shown by Vink that intestinal antisepsis increased the incidence of tumour growth at an anastomotic site in the colon and this project was undertaken to repeat and extend Vink's work. The authors point out that pre-operative intestinal antisepsis is used almost routinely in the surgery of malignant disease of the colon, and the relationship between intestinal antisepsis and the spread of tumours deserves serious consideration. The series of experiments has shown, first of all, that tumour cells can be implanted during anastomosis of the colon and subsequently produce tumour in the anastomotic line, and further, that tumour cells spilled during an open anastomosis of the colon will grow in the peritoneal cavity. Control of the bacterial flora of the colon plus increased trauma to the colon were shown to increase significantly the incidence of tumour growth in the anastomosis. These findings emphasize the desirability of finding an agent to combat the influence of antisepsis on tumour recurrence. "Chlorpactin XCB" was tested and, in this study, found not to be useful in controlling the spread of growth by implantation.

Swollen Arm after Radical Mastectomy.

G. D. TRACY *et alii* (*Aust. N.Z. J. Surg.*, February, 1961) state that though control of the malignant process is the main consideration in radical mastectomy, the disability which may follow the operation should also be borne in mind. Swelling of the arm, often accompanied by discomfort, disfigurement and loss of function, is a common sequel which is not often mentioned in reporting the results of radical mastectomy. The authors have studied the frequency of arm swelling after the operation in 106 cases, by the use of an accurate method of measuring arm volume. Swelling was clinically evident in 50 patients; in addition seven had temporary or intermittent swelling not present at the time of measurement, and six others had subclinical swelling. The evidence indicates that the swelling

is due to lymphatic oedema. As post-mastectomy lymphoedema may cause considerable distress, the authors advocate a positive treatment programme for these patients. They point out the value of arm-volume measurements in assessing the progress of the condition and the results of therapy.

Fate of Homografts and Prostheses of the Human Aorta.

B. HALPERT, M. E. DE BAKET *et alii* (*Surg. Gynec. Obstet.*, December, 1960) present a study of the structural alterations in 13 homografts of human aortas which had been in place from 24 to 80 months, and of the changes in 14 prostheses of human aortas which had been in place from 3 to 43 months. Of the 14 prostheses, one was of "Orlon", five were of "Nylon", and eight were of "Dacron". In the homografts, the changes were those of progressive attrition of the elastic fibres of the graft media, with apposition from the outside of hyalinizing fibrous connective tissue with coarse collagenous bundles. Sparse remains of the homograft were observed as long as 80 months after implantation. Of the 13 patients with homografts, four were still alive, portions of their grafts having been resected when by-pass operations were performed; of the nine who died, in three death was attributable to failure of the graft. In the prosthesis, the changes observed were those of progressive encasement by hyalinizing fibrous connective tissue. Of the 14 patients with prostheses, two were still alive, and in the other 12 the immediate cause of death was not associated with their prostheses. The authors state that the ideal prosthesis is still to be found, but that the knitted "Dacron" prosthesis appears to be satisfactory in most instances.

Jaundice Complicating Acute Cholecystitis.

F. Z. REINUS AND H. J. KESSELER (*Surgery*, September, 1960) review 84 patients with acute cholecystitis accompanied by jaundice. Of these patients, 24 had common duct stones. The authors point out that the degree of jaundice does not necessarily reflect the presence or absence of common duct stones, also that the exploration of the common duct is handicapped by the presence of acute inflammation. In the 23 patients found to have common duct stones, 9 were later found to have retained stones on cholangiography. Calculi were overlooked at the first operation in over one-third of these patients.

Reappraisal of Thoraco-Lumbar Sympathectomy for Essential Hypertension.

S. L. SCHWARTZ *et alii* (*Arch. Surg.*, July, 1960) evaluate the long-term (8 years at least) effects of thoraco-lumbar sympathectomy in 90 hypertensive patients. They found that the majority of patients did not achieve either a persistent decrease of diastolic pressure or significant relief of symptoms. A small percentage of patients, however, did show a dramatic and sustained reduction of blood pressure and relief of symptoms after operation.

Brush Up Your Medicine.

THE EARLY MANAGEMENT OF SEVERE TETANUS.

SEVERE TETANUS may be defined on the basis of a short incubation period of less than ten days and a rapid march of symptoms from trismus to severe and frequent reflex spasms in less than 48 hours. It must be emphasized that in the early stages a case may appear to be mild, but there ensues a steady relentless progression within the next few days.

A decision must be made at the earliest stage concerning the optimal site of treatment, which should be in a hospital equipped and prepared to treat severe tetanus; this demands intensive care for at least three to four weeks.

Transportation may be required, perhaps over long distances. Good ambulance transport will normally suffice; breakneck speed is not required, but over-cautiously reduced speeds are needlessly time-consuming. A doctor and nurse should be in constant attendance *en route* to supervise the early treatment; this would also apply to transport by air should this be readily available.

Immediate medical treatment should be instituted as soon as the diagnosis of tetanus is reasonably suspected. This consists of the intramuscular injection of crystalline penicillin, 1,000,000 units every six hours, and of tetanus antitoxin, 100,000 units in a single dose and not repeated, and sedation. For a person weighing 70 kg. (154 lb.) the following sedation is recommended: chlorpromazine, 100 mg. by intramuscular injection every four hours, and paraldehyde, 6 ml. by intramuscular injection every four hours. If paraldehyde is not available, "Sodium Amytal", 100 mg. by intramuscular injection, may be substituted. If practicable, a slow intravenous infusion of glucose-saline solution is advantageous, as it conveniently permits the intravenous administration of chlorpromazine.

In general, it is wisest to carry out all definitive surgical treatment at the elected hospital centre. Definitive surgical treatment consists of tracheostomy, *débridement*, and the insertion of a gastric tube under general anaesthesia. In rapidly advancing cases, emergency tracheostomy could be required before transport is undertaken; the anaesthetist should preferably be a person experienced in the use of relaxant drugs.

It is still controversial whether maintenance treatment of tetanus should be with relaxant drugs and assisted respiration. However, it is our present experience that even in severe cases the patient can be maintained with chlorpromazine and paraldehyde given by the intragastric drip method, as described by Maddocks and Dawborn in this issue, and by others, including Shanker and Mehrotra (1959) in India.

IAN J. WOOD,¹

IAN R. MACKAY,¹

Clinical Research Unit of the
Royal Melbourne Hospital and
the Walter and Eliza Hall
Institute of Medical Research,
Melbourne, Victoria.

Reference.

- SHANKER, A. and MEHROTRA, L. S. (1959), "A Preliminary Report on Chlorpromazine in Tetanus", *Brit. med. J.*, 2: 1150.

British Medical Association.

VICTORIAN BRANCH: SECTION OF PREVENTIVE MEDICINE.

A MEETING of the Section of Medicine of the Victorian Branch of the British Medical Association will be held on May 11, 1961, at 4.30 p.m., in the Medical Society Hall, 426 Albert Street, East Melbourne. Dr. K. F. Brennan will read a paper entitled "Popular Misconceptions Regarding the Present Status of Venereal Diseases". All those interested are invited to attend.

¹ Working with the aid of a grant from the National Health and Medical Research Council of Australia.

Out of the Past.

UNIVERSITY OF MELBOURNE.¹

[From the *Australasian Medical Gazette*, May 20, 1902.]

At the University Council meeting on April 14th, a letter was read from the Secretary for Agriculture, expressing the wish of the department that Dr. Cherry should be appointed dairy expert and bacteriologist to the department, while still retaining his position as lecturer in bacteriology. It was explained that Dr. Cherry had, up to the present, performed the bacteriological work of the department at the University, and that it was proposed to maintain and extend the work. The council expressed its general consent to the appointment, and empowered the finance committee to make the necessary arrangements. Dr. Morrison proposed that, in view of the great loss to medical education which the resignation of Dr. [C. J.] Martin, Acting Professor of Physiology, would cause to the University, he be urged to remain. He stated that Dr. Martin had received an offer from the Belfast University. After discussion in which it was stated that the loss of Dr. Martin would be disastrous to the University, it was decided that the chancellor be empowered to inform him that he would be treated liberally in the matter of leave of absence to make investigations abroad, and that it was the desire of the council that he should succeed to the chair of physiology.

Special Correspondence.

LONDON LETTER.

BY OUR SPECIAL CORRESPONDENT.

Health and Wealth.

MUCH CRITICISM has been expressed in the medical and lay Press on the subject of the increased charges for the National Health Service—namely, an increase in the weekly contribution and a charge of 2s. per item on prescriptions. Mr. Enoch Powell, the new Minister of Health, has claimed that the rises in N.H.S. contributions and charges will save £65,000,000 *per annum*, and that they will not impose any hardship or unreasonable burden. It has been generally assumed that the majority of the population in an affluent society will be able to pay up without any embarrassment to their pockets or habits, and that those who suffer hardship can receive aid from National Assistance. It is by no means clear how many people are at or near subsistence level. One suggestion is that they represent a "submerged fifth" of the population. No research has been undertaken to ascertain what will be the effects of the new increases. Financial expectations are largely guesswork, based on an annual fall in prescriptions, and also on the fact that doctors may prescribe larger quantities of drugs at a time. The cost of refunds in hardship cases is also uncertain.

The increased cost of prescriptions has been hardest on patients with chronic conditions, and both the British Diabetic Association and the British Epilepsy Association are very critical of the new imposition. Increased charges for dentures and spectacles may mean that those in need may be put off because of the cost. One report on family needs suggests that in about 14% of families with children aged under 16 years, treatment for eyes and teeth has not been undertaken. The Government assumes that increasing the cost of dentures will help to maintain the emphasis on conservative dentistry, but the British Dental Association feels that the rise will make no difference.

It seems likely that most people can afford the new health charges, but there is considerable ignorance as to their financial and moral effects in any detail.

Future of the Mental Hospitals.

The Government intends to spend £500,000,000 in the next ten years on new hospitals and on improving old ones. How this will affect the mental hospitals was announced by the Minister of Health at the annual conference of the National

¹ From the original in the Mitchell Library, Sydney.

Association of Mental Health in London in March. He startled his audience by saying that in 15 years' time there would be needed only half the number of places in mental hospitals, which in numerical terms he estimated as a redundancy of 75,000 beds, based on present trends. In the future, beds for mental patients will be, for the most part, in wards or wings of general hospitals; few will be in isolated institutions. This will mean the elimination of the greater part of the country's mental hospitals as they stand today. "The asylums which our forefathers built with such solidity". He emphasized their powers of resistance to assault. To those who declared that it would be a pity to waste all this hospital accommodation, the Minister declared that for the great majority of these establishments there is no appropriate future use, and he would resist any attempt to foist another purpose on them. Resistance to change will also come from the hundreds of men and women, professional or voluntary, who have given years, even a lifetime, to the service of a mental hospital. It will require no mean moral effort to recognize that the institutions are doomed. Finally, it will mean the transformation of a whole branch of medicine, of nursing and of hospital administration.

Speaking of hospital provision in general, the Minister stated that a hospital plan for the future would not make sense unless the medical profession outside the hospital service were able progressively to accept responsibility for more of the care of patients, which today is given inside hospitals. They would be supported in this task by a new development of the Local Authority services, more community care and more trained social workers.

Criticism of the Minister's proposals was widespread among the thousand delegates present. The view emerged that the plan to transfer the care of the mentally ill from the hospitals to the community was fraught with extreme dangers.

Happier Hospitals.

A report on hospital life, the pattern of the patient's day, comments forcibly on the iron Victorian discipline under which patients and staff still labour. This report, by the Standing Nursing Advisory Committee under the chairmanship of Miss Powell, Matron of St. George's Hospital, London, deals with hospital and ward routine, and much of present-day practice comes under criticism.

Rest is an essential part of the patient's treatment, yet it is becoming increasingly more difficult to rest in hospital. "The patient is called upon to endure a marathon, beginning from far too early in the morning and lasting until late in the evening." In many hospitals the patient's day begins sometime between 5 a.m. and 6 a.m. and ends between 9 p.m. and 10 p.m. The hospital should, as far as possible, aim to provide for the patient a life arranged on the basis of his home life. The hospital day should be planned around a basic timetable drawn up in the light of what most nearly corresponds to the normal routine of the greatest number.

Discussing ward routine, the Committee states that the major obstacle to be overcome seemed to be the tendency for such routine to be relatively inflexible. Many patients who are not seriously ill may receive almost as much individual attention as those who are gravely ill and absolutely dependent on the nursing staff. It is quite usual for all patients, whether or not they are able to get up, to have their beds made before breakfast as a matter of routine. Similarly, early morning sanitary rounds, distribution of hand-basins, etc., were among routine procedures, irrespective of whether the patients needed this degree of personal attention. It was hardly surprising that, when all these procedures had to be packed into a comparatively short space of time, the ward staffs found it impossible to contemplate a later start to the patients' day. It should never be normal practice to provide personal attention for all indiscriminately. The ward sister and her staff should seek to determine the degree of personal attention that each patient needs and arrange the ward routine accordingly. Suggestions made by the Committee were: (i) In many instances, beds need not be made more than once a day, and this can be left until later in the day when the patients are out of bed or attending to their toilet. (ii) Routine distribution of bed-pans and hand basins should be eliminated except for seriously ill patients. Once routine bed-making and sanitary rounds have been curtailed, flexibility in the time of waking becomes possible. (iii) Subject to medical opinion, the need for recording temperatures and pulse rates more than once a day is questioned. (iv) Relaxation of the present practice that all ward activity should cease during medical rounds would be a welcome contribution to ward efficiency. (v) While there is no objection to offering early morning tea to patients who

are awake, there is no justification for arousing the whole ward for "a ceremonial cup of tea". Meals should be so arranged that patients have the opportunity of one and a half hours' rest in the middle of the day. (vi) Visiting hours should be staggered, allowing two alternative sessions.

To a certain extent, the irritations of the daily timetable are a reflexion of the slow progress of hospital modernization, and the new and expanding hospital programme may go some way to meet this; but the Committee realizes that the traditional conservatism of the nursing profession is an obstacle to be overcome.

Human Relations in Obstetrics.

A similar report on the conditions in which some mothers are treated in maternity hospitals, by the Maternity and Midwifery Advisory Committee, has recently appeared. It gives as the commonest cause of dissatisfaction during the ante-natal period the long waiting time, spent in poor overcrowded premises, followed by a rapid examination with no privacy. Other complaints are the inadequate explanations of any abnormality which may have arisen, and the ignoring of minor worries such as morning sickness, backache and sleeplessness. During labour, the complaints are of being left alone, of the frightening effects of hearing other mothers in a more advanced stage of labour, of midwives acting as if the baby belonged to them and not the mother. In the puerperium, the complaints are of noise, being wakened unnecessarily early and the lack of day-room facilities.

Last year, Professor Norman Morris stated that the existing hospital system often failed miserably in the case of the patient's emotions. The joy, hopes and wonder that the arrival of new life should bring are spoiled and splintered into loneliness, indignity and despair.

The report lists the causes of the above-mentioned complaints as over-crowded premises, understaffing, changes in recent years of the attitude of patients, and lack of tolerance and understanding by the staff. At the core of the problem is the chronic inadequacy of the physical conditions and the shortage of midwives. Perhaps the more fundamental approach to the problem would be the encouragement of more confinements at home, or in small maternity units where the mother could be looked after by the family doctor. Mass production in huge maternity units must invariably lead to impersonal relationships.

Medical Staffing of Hospitals.

Since July, 1958, a Working Party under Professor Sir Robert Platt have been inquiring into the medical staff structure in the hospitals of the National Health Service. Evidence was taken from over 100 organizations and individuals, and hospitals were visited in England, Scotland and Wales. The staffing systems of other countries were also considered.

In the report, the Working Party state that the number of doctors in the hospital service in the various grades and specialties has risen in 10 years from 15,950 in 1949 to 20,950 in 1959 and the number of consultants from 5600 to 7700. They have evidence that work, properly belonging to consultant posts, has regularly been discharged by senior registrars and more junior grades. In spite of increase in consultant posts, the number is still inadequate.

The medical staff structure must be based on consultants, since doctors of consultant rank are recognized, and are the only doctors so recognized in the Health Service, as being qualified by training and experience to take full personal responsibility for the complete medical care of all patients within their particular specialty. To provide more permanent assistance for consultants, there should be new posts of the grade of "medical assistant" of unlimited tenure, both whole-time and part-time, for those who wish to make the hospital service their permanent career as well as for suitably experienced general practitioners. More openings for general practitioners are envisaged both as clinical assistants and as part-time medical assistants in the new grade.

At the present time, the junior staffs of the 3000 State hospitals are largely of Commonwealth or foreign origin. In surgery the proportion of junior doctors from overseas is as high as 59%. The Working Party do not ignore the probability of a decline in the number of overseas doctors as post-graduate training is developed in their own countries. Young British doctors might be persuaded to extend their hospital service. At present, 36% stay for less than two years.

This long and complicated report will be discussed by representatives of the hospital medical staffs all over the country and by the professional organizations.

Correspondence.

ERYTHROBLASTOSIS FETALIS—RANDOM THOUGHTS.

SIR: In a provocative article "Erythroblastosis Fetalis—Random Thoughts" (M^{rs}. J. Aust., March 18, 1961), Dr. Manion writes: "My remarks . . . are prefaced with an apology for the absence of particular or detailed knowledge of this subject." Later he writes: "How interesting it would be to have the time and facilities to investigate the maternal output of, say, foetal and urinary bile pigments in a mother, heavily sensitized with an incompatible pregnancy." I assume that your contributor means "faecal and urinary bile pigments", and I should like to comment that such investigations have been undertaken—by several clinical biochemists and others known to the present writer—with decidedly uninteresting results (see, for example, the experience of Waters¹). Furthermore, it is not difficult to see why this should be so when we consider: (i) the difference between the average volumes of maternal and foetal blood from which, presumably, bilirubin is derived (0.15 to 0.2 litre for a 2000 gramme foetus and 4.5 to 5.0 litres for a mother); (ii) the lack of reliable evidence that the erythrocytes in a normal foetus are more rapidly destroyed than those in adults; and (iii) the wide range of values normally obtained for 24 hour faecal excretion of urobilinogen (30 to 275 μ g.).

At the Royal Women's Hospital, Melbourne, using molecular absorption spectroscopy and a sensitive analytical method for bilirubin (Bruckner²), an investigation of the morning plasma pigment levels was undertaken weekly during the course of the last trimester of pregnancy. There were seven Rh-immunized patients. Three patients subsequently had normal, healthy babies. The plasma bilirubin of two of these fluctuated between 250 and 415 μ g. per 100 ml., while the other patient (gravida 18, para 11) had levels of 570 to 860 μ g. per 100 ml. Four patients who subsequently gave birth to infants with haemolytic disease (and requiring 0, 2, 2 and 3 exchange transfusions respectively) had bilirubin levels of 240 to 420 μ g. per 100 ml. It does not therefore appear that this approach to the problem of finding a reliable prognostic method for determining the probable fate of the baby is likely to succeed. Perhaps something more than "time and facilities" is required.

May I also explain, through the courtesy of your columns, why it is not at all "strange how the albumin-bound molecule (bilirubin) which cannot traverse the renal or hepatic barrier, has no difficulty with the placental barrier". Without going into the nature of the chemical bonds between biladienes and albumins, it is a fact that bilirubin in albumin-containing fluids can be transferred across a membrane impermeable to albumin, when there exists beyond that membrane a solution containing similar or greater concentrations of albumin.

Odell³ believes that the movement of pigment across membranes *in vivo* is determined by the degree of dissociation of the bilirubin-albumin complex—i.e., the concentration of non-protein-bound pigment. On this hypothesis, a low albumin and a high bile pigment content of foetal plasma would favour the dissociation of the bound pigment and, hence, the passage of bilirubin across the placenta. My own view is that bilirubin is transferred directly to the adult plasma albumin from the foetal protein through the placental membrane. Because the lumina of the renal tubules or bile capillaries contain no appreciable concentrations of soluble albumin nor any other receptors capable of attracting and holding the lipophilic pigment, bilirubin is not secreted.

Finally, on the subject of the solubility of bilirubin *in vitro*, pure bilirubin (which dissolves in water at pH 8) would normally be considered "insoluble" in neutral ethanol. This is contrary to the statement of Dr. S. E. J. Robertson (M^{rs}. J. Aust., March 18, page 401). However, the purpose of mentioning this is to draw attention to the fact that a method (King and Wootton⁴) described as "suitable" for the estimation of serum bile pigments is both inaccurate and poorly reproducible. This is due to the low solubility of

bilirubin and bilirubin esters in 80% ethanol at pH 4 to 5; both forms of pigment (but chiefly the ester form) may be co-precipitated with protein. Our experience leads us (Watson and Rogers⁵) to conclude that, at the present time, the non-precipitation method of Lathe and Ruthven⁶ is the only entirely satisfactory procedure for following the course of hyperbilirubinaemia in the new-born.

Yours, etc.,

Royal Women's Hospital,
Melbourne.
March 28, 1961.

D. WATSON, F.R.I.C.,
Biochemist.

FREQUENCY OF COMPULSORY MEDICAL EXAMINATIONS UNDER N.S.W. WORKERS' COMPENSATION RULES.

SIR: I have recently learned something from the following letter to me which I feel worth publishing for the benefit of New South Wales practitioners.

The Workers' Compensation
Commission of N.S.W.,
Sydney.
3rd March, 1961.

Dear Sir,

I desire to acknowledge receipt of your letter of the 9th instant and to advise that the Workers' Compensation Act and the Rules made thereunder make provision regarding the frequency of examination by a medical practitioner.

In cases where the worker is not in receipt of weekly payments but has given notice of an injury he can be required to submit himself to as many examinations as the employer may reasonably require. In default of agreement between the parties on this point the matter would then have to be determined by the Commission in the ordinary way.

Where, however, the worker is in receipt of weekly payments the Rules provide that he shall not be required, after a period of one month has elapsed from the date on which the first payment of compensation was made, or if the first payment is made in obedience to an award of the Commission from the date of the award, to submit himself against his will for examination by a medical practitioner provided by the employer except at the following intervals:

Once a week during the second and once a month during the third, fourth, fifth and sixth months after the date of the first payment of the award, as the case may be, and thereafter once in every two months.

Yours, faithfully,
H. LEROD,
Registrar.

The principles embodied may well have more general application; I see in such principles a close relationship to the preservation of future private practice against State control. Perhaps the general subject of workers' compensation medico-legal problems as seen from all angles might merit the attention of the new Medico-Legal Society.

143 Macquarie Street,
Sydney.
April 10, 1961.

Yours, etc.,
C. C. McKellar.

FURALTADONE—A CLINICAL TRIAL.

SIR: In his letter to your Journal (April 8, 1961), Dr. Godfrey referred to furaltadone,¹ as a "potentially dangerous substance", and that "trials elsewhere have not suggested that it will have a useful place in the treatment of staphylococcal infections. . . ."

The neurotoxicity of furaltadone referred to by Dr. Godfrey has been the subject of intensive investigation, and in the United States reports of 69 such cases have been recorded. These, in an estimated total of 900,000 courses of therapy, amount to an incidence of less than 0.01%. In these cases the average duration of furaltadone administra-

¹ J. clin. Path., 1961, in the press.

² J. clin. Path., 1958, 11:155.

³ Furaltadone is marketed under the trade name "Altafur".

¹ Quoted by Schmid, R., Buckingham, S., Hanmaker, L., and Mederilla, G. (1959), *Amer. J. Dis. Child.*, 1959, 98: 631.

² *Amer. J. clin. Path.*, 1959, 32: 513.

³ *J. Pediatr.*, 1959, 55: 268.

⁴ "Micro-analysis in Medical Biochemistry", 1956, Churchill, London.

tion required to produce these effects was 38 days, with a range of from two to 210 days. On withdrawal of the drug, the effects completely subsided in 61 of these patients. Continuing improvement is being shown by six, whilst one patient, a chronic alcoholic, has loss of taste, and another a diminished auditory acuity.

With regard to the efficiency of furaltadone as an antibacterial we should like to point out that published papers to date report on 1225 patients, of whom 74% were cured by this drug. A number of these authors have commented on the value of furaltadone in staphylococcal infections. MacLeod¹ reports that Eaton Laboratories have on record 4237 case reports, of which furaltadone cured 56% and improved 23%. Previous antibacterial therapy had been unsuccessful in 704 of this total, and of these furaltadone cured 47% and improved 29%.

Yours, etc.,

R. K. WYBURN,

Managing Director.

Smith, Kline & French Laboratories
(Aust.) Ltd.,
Cnr. Denison and Spring Streets,
North Sydney.
April 11, 1961.

STORAGE AND SUPPLY OF IMMUNIZING MATERIAL.

SIR: It is with some hesitation that I would pursue the controversy of polio and tetanus vaccines further. However, while the information provided by Dr. Bazeley was very useful, his letter went far short of a satisfactory answer to some of my original questions.

Dr. Bazeley seems loath to answer the simple question: "Is tetanus toxoid as liable to deterioration as polio vaccine?" This may appear pedantic; but the point is surely that two standards are being demanded, one for polio and another for tetanus prophylactic; why?

Dr. Bazeley surely begs the question when he states: "We feel certain that the many persons already immunized with tetanus toxoid can be assured of immunity, provided the preparation is not kept for long periods under adverse conditions." I am suggesting that these products have been and still are being kept under adverse conditions. Indeed, when asked about his tetanus toxoid, one chemist stated that, as long as it was kept in the temperature prevailing in his shop, it would keep for two years. This seems to be at considerable variance with Dr. Bazeley's recommendations.

Finally, I do not think it is asking too much to expect Commonwealth Serum Laboratories to show the same interest in regard to storage of tetanus toxoid (in particular) as they are showing in the case of polio vaccine, as the present state of affairs in regards to tetanus toxoid seems to fall far short of Dr. Bazeley's recommended requirements.

Yours, etc.,

LIONEL L. WILSON.

80 Penshurst Street,
Penshurst,
New South Wales.
April 6, 1961.

SIR: The recommended storage temperatures for vaccines are as follows: (i) triple antigen, 2° to 4° C.; (ii) tetanus toxoid, 0° to 5° C.; (iii) tetanus antitoxin, 0° to 5° C.; (iv) influenza virus vaccine, 2° to 10° C.; (v) Salk vaccine, 0° to 2° C.; (vi) quadruple antigen, 0° to 2° C.; (vii) smallpox virus, minus 10° C. Except for smallpox, these vaccines must not be frozen.

Studies performed with a maximum-minimum mercury thermometer wrapped in a transparent plastic bag and exposed to the air in the domestic refrigerator in Brisbane in March, 1961, show the following temperature ranges: (i) Model A: door shelves, 10° to 15° C.; meat tray, 3° to 5° C.; shelf beneath meat tray, 5° to 10° C. (ii) Model B: a small refrigerator used entirely for vaccine storage, 4° to 17° C. There is good reason to believe that the recorded air temperatures approximate to the actual vaccine temperature. Thus the existing models of domestic refrigerators are not ideal for vaccine storage.

A firm of refrigerator manufacturers in Brisbane designed a model suitable for storage of blood and serum for use

in country hospitals. This model consists of a more powerful freezing unit than is usual in domestic refrigerators, a fan to distribute uniformly the cooled air from the unit throughout the cabinet, and a sensitive thermostat which will control the internal temperature within a range of 20° C. Unfortunately this model is large and expensive, and has a side-opening door. Therefore, there is need for a new design, and a model is being designed which will incorporate the unit described in the base of a cabinet of two cubic feet capacity with a top opening door to eliminate the loss of cool air when the door is opened. The vaccines will be stored in metal baskets. It can be predicted that this model will prove suitable for vaccine storage. It is hoped that the cost will be not more than £120. A full report will be forwarded when the model is built, and the trials completed.

Yours, etc.,

R. F. O'SHEA.

51 Wickham Terrace,
Brisbane,
Queensland.
April 10, 1961.

SIR: I was surprised to read a further reminder in the current Monthly Bulletin of the New South Wales Branch of the British Medical Association to store tetanus toxoid and tetanus prophylactic in a refrigerator, and to ensure that all supplies of these are similarly stored. Surely the latter is the duty of the Health Department, not of general practitioners. In any case, how can we do this, as we have no knowledge of what happens to these vaccines between their leaving the factory and their arrival at the chemist?

It seems to me that the B.M.A. would be better advised to do something about shaking up the Health Department to act in the matter. At the same time, it might not be out of place to point out that the same rules for storage apply to all vaccines, not just those mentioned, and of course other biological products.

There is, of course, a very satisfactory alternative—namely, to do away with the need for prescriptions for these products, so that medical practitioners can order directly from the manufacturers—and to blaze with any irresponsible middle men!

Yours, etc.,

T. G. BROWN.

Weddin Street,
Grenfell,
New South Wales.
April 15, 1961.

HYPERTENSION AND LIFE ASSURANCE.

SIR: Referring to Dr. McCristal's letters under this head in THE MEDICAL JOURNAL OF AUSTRALIA of February 25 and April 1, 1961, it appears that "we" doctors cannot escape his suggestion that we may "fudge and fabricate blood pressure readings". He says: "One finds the higher initial blood-pressure readings—e.g., 160/95—glossed over and discarded in favour of the lower figures."

I had always thought that the truest reading was taken on a recumbent patient after 10 minutes' rest. As this may be time-wasting, I take a quick reading with patient sitting, and if this is normal that ends the matter. If it is too high, I record it, but go on to resting, sitting or recumbent readings, and record these. The lowest reading obtained I take to be the true reading. Nothing contrary to this interpretation appears in the "Notes for Medical Examiners" issued by the Life Offices Association for Australasia in July, 1947.

If this is fudging, I am open to correction, but if something worse is implied, then I think Dr. McCristal and I will plead "not guilty", and have to search among the 4% of unreliable who, I understand, are to be found in any calling.

If, indeed, some of us are not playing the game, I hope that the sinners will pause to think that, if a time should come when we have to seek an increase in the presently quite adequate fee paid for a life assurance examination, then we may find the life assurance companies as un-cooperative as we find governments at such a time.

Yours, etc.,

J. WOOLNOUGH.

35 Oxford Street,
Epping,
New South Wales.
April 10, 1961.

¹ New Engl. J. Med., 1961, 264: 517.

Post-Graduate Work.

THE POST-GRADUATE COMMITTEE IN MEDICINE IN THE UNIVERSITY OF SYDNEY.

Annual Subscription Course.

The following lectures are open to members of the annual subscription course.

Wednesday, May 3: 2 p.m., "Gall-Stones and Their Consequences", Mr. Hedley Atkins, Maitland Lecture Hall, Sydney Hospital; 8.15 p.m., "Treatment of Carcinoma of the Breast", Stawell Hall, 145 Macquarie Street, Sydney.

Thursday, May 4: 8.30 p.m., Third John Irvine Hunter Memorial Oration, Professor Bradley M. Patten.

Friday, May 5: 5 p.m., "The Aetiology of Prematurity", Professor Nillo Hallman, Main Lecture Theatre, Royal Alexandra Hospital for Children.

Monday, May 8: 5 p.m., "The Influence of Hospitalization on Children", Professor Nillo Hallman, Main Lecture Hall, Royal Alexandra Hospital for Children.

Wednesday, May 10: 8.15 p.m., "Breast Diseases in General Practice", Mr. Hedley Atkins, Stawell Hall, 145 Macquarie Street, Sydney.

Monday, May 15: 8.15 p.m., "Endocrine Influences on Growth", Professor Douglas Hubble, Main Lecture Hall, Royal Alexandra Hospital for Children.

Tuesday, May 16: 4 p.m., "Endocrine Disorders in Childhood", Professor Douglas Hubble, Main Lecture Hall, Royal Alexandra Hospital for Children.

Wednesday, May 17: 8.15 p.m., "Common Injuries in Sport", Mr. Hedley Atkins, Stawell Hall, 145 Macquarie Street, Sydney; 8.15 p.m., "Steatorrhoea in Childhood", Professor Douglas Hubble, Main Lecture Theatre, Royal Alexandra Hospital for Children; 8 p.m., "Starling's Law—Digitalis and Myocardial Oxygen Consumption", Dr. Eugene Braunwald, Maitland Lecture Hall, Sydney Hospital.

Thursday, May 18: 8.15 p.m., "Accident and Design in Surgery", Professor T. Cecil Gray, Stawell Hall, 145 Macquarie Street, Sydney (in association with the Faculty of Anaesthetists, N.S.W. State Committee, Royal Australasian College of Surgeons).

The annual subscription course covers attendance at lectures by overseas lecturers and other specially arranged activities. The annual fee is £3 3s., from July 1. The fee for first-year and second-year resident medical officers is £1 12s. 6d. Last-minute alterations to meetings are notified by advertisement in *The Sydney Morning Herald* ("Public Notices"), if possible on the day before the meeting.

Course in Clinical Respiratory Physiology.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a course in clinical respiratory physiology will be conducted in the Department of Medicine, University of Sydney, from Tuesday, June 6, to Thursday, July 6, 1961, under the supervision of Dr. John Read. It will consist of ten sessions of a lecture-demonstration-discussion nature, lasting from one to one and a half hours, and beginning at 4 p.m. on Tuesdays and Thursdays. The programme is as follows:

Tuesday, June 6: Introduction, "The Gas Laws", Dr. John Read and Dr. K. T. Fowler.

Thursday, June 8: "Blood Gases and pH", Dr. John Read and Dr. K. T. Fowler.

Tuesday, June 13: "Ventilation of the Lungs", Dr. John Read.

Thursday, June 15: "Ventilation-Blood Flow Relationships", Dr. John Read, Dr. K. T. Fowler and Dr. K. L. Cotton.

Tuesday, June 20: "Blood Flow, with Particular Reference to the Pulmonary Circulation", Dr. K. L. Cotton.

Thursday, June 22: "Diffusion", Dr. K. T. Fowler and Dr. John Read.

Tuesday, June 27: "Mechanics of Breathing", Dr. K. T. Fowler and Dr. John Read.

Thursday, June 29: "Changes in Ventilation", Dr. K. L. Cotton.

Tuesday, July 4, and Thursday, July 6: discussion of individual phenomena and disease patterns; practice interpretation of results.

The fee for attendance is £5 5s., or £2 2s. for full-time hospital registrars. Early enrolment is essential, and should

be made with the Course Secretary of the Post-Graduate Committee in Medicine, from whom programmes may be obtained.

Course in Anaesthetics for General Practitioners.

A course in anaesthetics will be conducted by the Department of Anaesthetics and Resuscitation at the Sydney Hospital for two weeks from November 13 to 24, under the supervision of Dr. Douglas Joseph. The course will be full-time from 9 a.m. to 6 p.m. daily, consisting of practical demonstrations and tutorials. Enrolments will be limited to four, and applicants should submit particulars of their anaesthetic experience and requirements. It is regretted that, for the present, this course is open only to applicants from New South Wales. The closing date for applications is June 30, 1961, and the selection of candidates will be announced shortly after this date. The fee for attendance is £12 12s., payable after selection date. Application should be made on the prescribed form, which is available from the Committee.

Course in Advanced Medicine.

A three months' course in advanced medicine suitable for candidates for the M.R.A.C.P. examination will begin on June 5. It will consist of lectures, demonstrations and ward rounds held in the afternoons only.

Course for D.P.M. Part I.

A Part I course for the Diploma in Psychological Medicine will begin on June 5 and continue for a period of eight months. The fee for attendance is 50 guineas.

Method of Enrolment.

Applications to attend any of these courses should be made to the Course Secretary, The Post-Graduate Committee in Medicine, Herford House, 188 Oxford Street, Paddington, New South Wales. Telephone: FA 0671. Telegraphic address: "Postgrad Sydney".

Taxation Deductions.

Fees paid by medical practitioners, who are in practice, for attendance at revision and week-end courses conducted by the Committee, including living and travelling expenses, are deductible (Taxation File No. AF/1865).

Post-Graduate Conference on Obstetrics and Gynaecology at Newcastle.

The Post-Graduate Committee in Medicine in the University of Sydney announces that a week-end conference will be conducted at Newcastle in conjunction with the Central Northern Medical Association on Saturday, May 6, 1961. The conference will be held in the S.35 Room of the Technical College, Maitland Road, Tighes Hill, and the programme is as follows. 2 p.m., registration; 2.15 p.m., "New Ideas on Old Problems in Sterility", Dr. Alan Grant; 3.20 p.m., "Carcinoma of the Cervix and Vaginal Exfoliative Cytology", Dr. Murray Moyes; 4.40 p.m., "Problems of Difficult Parturition", Dr. R. B. C. Stevenson.

The fee for attendance will be £2 2s., and those wishing to attend are requested to notify Dr. R. V. Dan, Honorary Secretary, Central Northern Medical Association, 17 Bolton Street, Newcastle, as soon as possible. Telephone: Newcastle B 2244.

Coming Events.

The Post-Graduate Committee in Medicine in the University of Sydney announces the following coming events.

The fourteenth Annual Post-Graduate Oration will be delivered by Dr. Keith Bowden on Thursday, May 11, at 8.15 p.m., in the Great Hall of the University of Sydney. The subject will be "George Bass".

The annual general revision course will be held from Monday, May 8, to Friday, May 19.

Overseas Visitors.

The following overseas visitors will be arriving shortly: Professor E. G. L. Bywaters, Empire Rheumatism Council Professor of Rheumatology, Postgraduate Medical School, University of London, Honorary Consultant Physician, Hammersmith Hospital, Honorary Consultant Physician, Canadian Red Cross Memorial Hospital, Taplow, England (April 22 to 27); Professor J. T. Ingram, Professor of Dermatology, University of Durham (April 26 to May 3); Professor Nillo Hallman, Professor of Pediatrics, University of Helsinki, Finland, and 1961 Pfizer Lecturer to the Australian Paediatric Association (April 29 to May 11); Mr. Hedley Atkins, Dean of the Institute of Basic Medical

Sciences and Director of the Surgical Department, Guy's Hospital, London, Sims Commonwealth Travelling Professor for 1961 to the Royal Australasian College of Surgeons (May 1 to 18); Professor T. Cecil Gray, Professor of Anaesthetics, University of Liverpool, Sims Commonwealth Travelling Professor for 1961 to the Royal Australasian College of Surgeons; Professor Bradley M. Patten, Emeritus Professor and Chairman of the Department of Anatomy, University of Michigan Medical School, U.S.A. (May 4 to 13); Professor Douglas Hubble, Professor of Pediatrics and Child Health, University of Birmingham (May 13 to 22); Dr. E. Harry Botterell, Chief of the Neurosurgical Division, Toronto General Hospital, Canada (May 13 to 20).

THE MELBOURNE MEDICAL POST-GRADUATE COMMITTEE.

Course in Medicine at the Alfred Hospital, Melbourne.

THE Honorary Medical Staff of the Alfred Hospital, Melbourne, will conduct a post-graduate course in medicine suitable for candidates sitting for the degree of M.D. (Melbourne) or the M.R.A.C.P. diploma. This will be a full-time course, and will run for eight weeks from June 5, 1961. The course will consist of lectures, discussions, case presentations, and seminars on radiology, morbid anatomy, clinical pathology, electrocardiography, modern investigatory techniques, etc. Enrolments, together with the fee of £31 10s., should be sent by May 22, 1961, to the Melbourne Medical Post-Graduate Committee, 394 Albert Street, East Melbourne.

CARDIAC SOCIETY OF AUSTRALIA AND NEW ZEALAND.

Visit of Dr. Eugene Braunwald to Melbourne.

DR. EUGENE BRAUNWALD will be visiting Australia as the R. T. Hall Overseas Lecturer for the Cardiac Society of Australia and New Zealand for 1961. He is Chief of the Cardiology Branch of the National Heart Institute, Bethesda,

Maryland, U.S.A. The following information relates to his Melbourne programme.

Wednesday, May 10: visit to the Alfred Hospital.

Thursday, May 11: visit to the Royal Children's Hospital; lecture to the Victorian Cardiac Group at 8.15 p.m., at the Royal Melbourne Hospital, "Studies on Starling's Law of the Heart, Digitalis, Myocardial Oxygen Consumption and Coronary Blood Flow" (all members of the medical profession invited to attend).

Friday, May 12: visit to Royal Melbourne Hospital, to take part in clinical discussions and deliver lectures on special techniques in cardiac investigation.

Further details may be obtained from Dr. J. M. Gardiner, 421 St. Kilda Road, Melbourne. Telephone: 26 5689; residence, 20 3166.

Notes and News.

The Priory of the Venerable Order of St. John of Jerusalem in Australia.

DR. G. G. L. STENING, of Sydney, has been appointed Chancellor of the Priory of the Venerable Order of St. John of Jerusalem in Australia. He succeeds Sir Hugh Poate, who died on January 26, 1961.

Uniform Registration of Medical Practitioners.

The Commonwealth Director-General of Health, Major-General W. D. Refshauge, has announced that preliminary steps have been taken towards securing uniform conditions of registration of medical men in the various States and Territories of the Commonwealth, and also uniform requirements in relation to the legal aspects of medical practice and professional conduct. The questions were discussed at a meeting in Canberra of the presidents and registrars of the Medical Boards of each State and the Australian Capital Territory. This was the first conference of Medical Boards since 1953. It was proposed that the Boards should confer regularly in future, meeting in the capital cities of the respective States. Dr. Cotter Harvey (Sydney) presided at

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED MARCH 25, 1961.*

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism
Amebiasis
Ancylostomiasis	9	..	9
Anthrax
Bilharziasis
Brucellosis
Cholera
Chorea (St. Vitus)
Dengue
Diarrhoea (Infantile)	12(9)	6(5)	2	8	..	28
Diphtheria
Dysentery (Bacillary)	1(1)	2	1(1)	1	..	1	..	6
Encephalitis
Filariasis
Homologous Serum Jaundice
Hydatid	119(41)	42(20)	15(3)	45(26)	9(6)	10(1)	2	5	247
Infective Hepatitis
Lead Poisoning	2	2
Leprosy
Leptospirosis	3	3
Malaria
Meningococcal Infection
Ophthalmia
Ornithosis	1	1
Paratyphoid
Plague
Polio-myelitis	1	2	3
Puerperal Fever	3	3
Rubella	8(5)	..	3(2)	4(2)	15
Salmonella Infection	1(1)	1(1)	..	1	2	4
Scarlet Fever	7(4)	10(7)	1(1)	3(1)	1	3	31
Smallpox
Tetanus	1	1
Trachoma	2(2)	..	1	..	3
Trichinosis
Tuberculosis	13(8)	10(9)	6(2)	3(5)	2	3(1)	5	..	42
Typhoid Fever	1(1)	1
Typhus (Flea-, Mite- and Tick-borne)	2	2
Typhus (Louse-borne)
Yellow Fever

* Figures in parentheses are those for the metropolitan area.

the conference, which was formally opened by the Commonwealth Minister for Health, Dr. Cameron. General Refshauge said that the conference suggested the creation of a General Medical Council of Australia to promote uniform policies in an advisory capacity. The primary aim of the Council would be to ensure adequate educational standards in all Australian university medical schools. Later it was hoped to extend the Council's functions to the establishment of uniform conditions for registration in all States, uniform reciprocity with overseas countries and uniformity in the admission of foreign graduates. The conference adopted a definition of medical specialists, to be referred to the individual Medical Boards for discussion and suggested adoption. Steps were also proposed to provide registration without fee for Service medical officers registered to practise only in a particular State or Territory.

The College of Radiologists of Australasia.

EXAMINATIONS FOR DIPLOMA.

THE College of Radiologists of Australasia will be holding examinations for Part I and Part II of the diploma of the College commencing on Monday, August 21, 1961. The examination for Part I is held in the candidate's own State, and that for Part II will be held in Sydney. Full details and application forms are available from the office of the College, 12th Floor, 135 Macquarie Street, Sydney. Entry forms must be received at the College office in Sydney not later than June 26, 1961.

Notice.

THIRD JOHN IRVINE HUNTER MEMORIAL ORATION.

THE third John Irvine Hunter Memorial Oration, arranged by the Post-Graduate Medical Foundation in the University of Sydney, the Children's Medical Research Foundation and the Department of Anatomy, University of Sydney, will be delivered at 8.30 a.m. on Thursday, May 4, 1961, in the Wallace Theatre, University of Sydney. The orator will be Professor Bradley M. Patten, Emeritus Professor and Chairman of the Department of Anatomy, University of Michigan Medical School, and he will take as his subject "First Heart Beats—The Beginning of the Embryonic Circulation". All interested persons are invited to attend.

Nominations and Elections.

THE undermentioned have applied for election as members of the New South Wales Branch of the British Medical Association:

Hamilton, Peter, M.B., B.S., 1961 (Univ. Sydney), Royal North Shore Hospital, St. Leonards.
James, Alan Ashley, M.B., B.S., 1958 (Univ. Sydney), 66 Raglan Street, Manly.
Shea, Peter Barry, M.B., B.S., 1961 (Univ. Sydney), District Hospital, Marrickville.
Nelson, David Selwyn, M.B., B.S., 1960 (Univ. Sydney), Department of Experimental Pathology, Australian National University, Canberra.

The following have applied for election as members of the South Australian Branch of the British Medical Association.

Maddern, Max Wilfred, M.B., B.S., 1960 (Univ. Adelaide), Queen Elizabeth Hospital, Woodville.
Rice, John Peter, M.B., B.S., 1960 (Univ. Adelaide), 117 Kensington Road, Norwood.
Krieger, Geoffrey Edward, M.B., B.S., 1960 (Univ. Adelaide), 15 Richman Avenue, Prospect.
Foy, Bryan Nelson, M.B., B.S. (London), M.R.C.O.G., 4 Lansell Street, Mt. Gambier.
Rutter, John Lyall, M.B., B.S., 1957 (Univ. Adelaide), Evans Street, Angaston.

Deaths.

PURVES.—Allan Melrose Purses, at Sydney.

Diary for the Month.

- MAY 2.—New South Wales Branch, B.M.A.: Organization and Science Committee.
- MAY 3.—Western Australian Branch, B.M.A.: Branch Council.
- MAY 3.—Victorian Branch, B.M.A.: Clinical Meeting (at the Austin Hospital).
- MAY 4.—South Australian Branch, B.M.A.: Council Meeting.
- MAY 9.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
- MAY 11.—New South Wales Branch, B.M.A.: Public Relations Committee.
- MAY 12.—Queensland Branch, B.M.A.: Council Meeting.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

ALL articles submitted for publication in this Journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations, other than those normally used by the Journal, and not to underline either words or phrases.

Authors of papers are asked to state for inclusion in the title their principal qualifications as well as their relevant appointment and/or the unit, hospital or department from which the paper comes.

References to articles and books should be carefully checked. In a reference to an article in a journal the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of article. In a reference to a book the following information should be given: surname of author, initials of author, year of publication, full title of book, publisher, place of publication, page number (where relevant). The abbreviations used for the titles of journals are those of the list known as "World Medical Periodicals" (published by the World Medical Association). If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full data in each instance.

Authors submitting illustrations are asked, if possible, to provide the originals (not photographic copies) of line drawings, graphs and diagrams, and prints from the original negatives of photomicrographs. Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary is stated.

All communications should be addressed to the Editor, THE MEDICAL JOURNAL OF AUSTRALIA, The Printing House, Seamer Street, Glebe, New South Wales. (Telephones: MW 2651-2-3.)

Members and subscribers are requested to notify the Manager, THE MEDICAL JOURNAL OF AUSTRALIA, Seamer Street, Glebe, New South Wales, without delay, of any irregularity in the delivery of this Journal. The management cannot accept any responsibility or recognize any claim arising out of non-receipt of journals unless such notification is received within one month.

SUBSCRIPTION RATES.—Medical students and others not receiving THE MEDICAL JOURNAL OF AUSTRALIA in virtue of membership of the Branches of the British Medical Association in Australia can become subscribers to the Journal by applying to the Manager or through the usual agents and booksellers. Subscriptions can commence at the beginning of any quarter and are renewable on December 31. The rate is £6 per annum within Australia and the British Commonwealth of Nations, and £7 10s. per annum within America and foreign countries, payable in advance.